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**LIVER AND BILIARY I – POSTER EXHIBITION**

## P0001 THE PROTECTIVE EFFECT OF BERAPROST SODIUM IN MONOCROTALINE-INDUCED SINUSOIDAL OBSTRUCTION SYNDROME IN MICE

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**Introduction:** Sinusoidal obstruction syndrome (SOS) is a drug-induced liver injury caused by anticancer treatments, such as oxaliplatin-based chemotherapy. Injury of sinusoidal endothelial cells (SECs) and subsequent extravasated platelet aggregation (EPA) initiate development of SOS. Beraprost sodium (BPS) has a protective effect on SECs and antiplatelet effect. The aim of this study was to examine the protective effect of BPS against SECs injury resulting from monocrotaline (MCT)-induced SOS in mice.

**Aims & Methods:** SOS was induced in Crl:CD1 (ICR) mice by intraperitoneal administration of MCT (270 mg/kg). To evaluate the effect of BPS on SOS, the mice were divided into two groups. In the BPS group, BPS (200 $\mu$l/kg) was injected by intraperitoneal administration at 1 hour before, 3 hours after, and 9 hours after MCT administration. The control group received intraperitoneal injections of the same volume of saline at the same time points. All mice were sacrificed at 48 hours after MCT administration and the protective effect on SECs was assessed by determining blood cell count, serum biochemical findings and immunohistochemical stains of sinusoidal endothelial cell antibody (SEC-1) and CD62P (P-selectin). Western blot analysis and real-time polymerase chain reaction (RT-PCR) were also used to examine plasminogen activator inhibitor-1 (PAI-1) and endothelial nitric oxide synthase (eNOS) expression.

**Results:** Platelet count was maintained in the BPS group compared to that in the MCT group (48.2 vs. 4.8 $\times 10^4/\mu$l, $P < 0.001$). Serum transaminase levels and hyaluronic acid (HA) in the BPS group were significantly reduced compared to the levels in the MCT group (AST 129 vs. 1013 IU/L, $P < 0.05$; ALT 90 vs. 923 IU/L, $P < 0.01$; HA 670 vs. 2243 ng/mL, $P < 0.01$). In the MCT group, liver histology showed endothelial damage of the central venule, congestion and obstruction of the sinusoids, and necrosis of hepatocytes in zone 3. In the BPS group, these findings were suppressed. Immunohistochemistry showed a protective effect of SECs on SEC-1 and a decrease in platelet infiltration in the space of Disse on CD62P in the BPS group compared to that in the MCT group. Expression of PAI-1 was significantly lower and expression of eNOS was significantly higher in the BPS group.

**Conclusion:** BPS preserved SECs and suppressed the progression of MCT-induced SOS in mice, suggesting that BPS is useful for the prevention of SOS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0002 HEPATOCYTE-SPECIFIC DELETION OF HYPOXIA INDUCIBLE FACTOR-2A ATTENUATES FIBROGENIC PROGRESSION IN MICE WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** Hypoxia and hypoxia inducible factors (HIFs) have been implicated in the fibrogenic progression of human and experimental chronic liver diseases, with HIF-1$\alpha$ originally suggested to play a role in the murine models of bile duct ligation and chronic diethylnitrosamine administration. Recently, a mechanistic study based on alternate hepatocyte-specific deletion of HIFs suggested that HIF-2$\alpha$ (rather than HIF-1$\alpha$) may sustain lipid accumulation and liver fibrogenesis in a short-term (two weeks) model of ethanol-related steatohepatitis.

**Aims & Methods:** Since increased HIF-2$\alpha$ expression has been observed in either experimental or human conditions of non-alcoholic fatty liver disease (NAFLD), the present study has been designed to mechanistically investigate the putative pro-fibrogenic role of HIF-2$\alpha$ in experimental NAFLD. Expression and the mechanistic role of HIF-2$\alpha$ have been investigated by means of morphological and molecular biology approach in the methionine/choline deficient diet (MCD) murine model of progressive NAFLD by employing i) wild type C57Bl6J mice and ii) mice carrying hepatocyte-specific conditional deletion of HIF-2$\alpha$ (HIF-2$\alpha$ fl/fl /Alb-Cre mice) vs related littermate (HIF-2$\alpha$ fl/fl mice).

**Results:** HIF-2$\alpha$ hepatic transcript levels were progressively up-regulated during the development of MCD murine model of NASH in parallel with the development of fibrosis, with increased expression being observed by immunohistochemistry mostly in hepatocytes. However, HIF-2$\alpha$ deficiency resulted in: i) a significant decreased expression of major pro-fibrogenic genes, including transforming growth factor $\beta$1, $\alpha$-smooth muscle actin, collagen 1A1, matrix-metalloprotease 2; ii) deleted expression of SerpinB3, a hypoxia and HIF-2$\alpha$-dependent mediator able to directly modulate pro-fibrogenic activity of HSC which is mainly released by hepatocytes in chronic liver diseases. Of interest, no significant up-regulation was observed for HIF-1$\alpha$ levels in mice carrying hepatocyte-specific deletion of HIF-2$\alpha$.

**Conclusion:** Hepatocyte-specific down-regulation of HIF-2$\alpha$ negatively affect liver fibrogenesis, suggesting that a HIF-2$\alpha$-dependent mediator released by hepatocytes like SerpinB3 may have a role in the fibrogenic progression of experimental NAFLD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0004 PROSPECTIVE COMPARISON OF NONINVASIVE TECHNIQUES FOR THE ASSESSMENT OF LIVER STIFFNESS IN A COHORT OF COMPENSATED HCV LIVER CIRRHOSIS

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**Introduction:** It is known that the liver biopsy is the gold standard for diagnosing liver fibrosis, but it also can be diagnosed by means of noninvasive techniques, either biological tests or ultrasound based elastographic techniques.

**Aims & Methods:** The aim of this study was to compare the performance of elastographic techniques and biological tests in diagnosing compensated HCV liver cirrhosis. We performed a prospective study, including 100 consecutive patients diagnosed with HCV liver cirrhosis. All patients were evaluated by point ultrasound shear wave elastography (SWE) – {Virtual Touch Quantification [ (VTQ)-Acuson S2000, Siemens], ElastPQ- (Affinity, Philips)}, by Transient Elastography [ (TE)-FibroScan, EchoSens], by 2-dimensional (2D) shear wave elastography (SWE)- [Aixplorer, Supersonic Imagine (SSI)], LOGIC E9 [GE Healthcare, Chalfont St. Giles-UK (2D-SWE GE)]-in the same session, while biological test (FibroTest) was performed within a month. In each patient we performed 10 valid measurements (VM) for TE, VTQ, ElastPQ and 2D-SWE.GE, and 3 for SSI. The following published cut-offs were used to diagnose cirrhosis: TE-12 kPa (1); VTQ-1.81 m/s (2); ElastPQ-12 kPa (3); SSI-13.5 kPa (4); 2D-SWE.GE-12 kPa (5).

**Results:** Our cohort included 100 subjects (60 women and 40 men), mean age of $60 \pm 5.3$, BMI $24.9 \pm 2.2$. Reliable LS measurements by means of point elastography were obtained in 100/100 subjects, by means of TE in 94/100 subjects (94%) and by means of 2D-SWE elastography in 87/100 subjects (87%), so the final analysis included 87/100 subjects (87%). TE elastography had 94.6% accuracy, point elastography – 79.3%, 2D-SWE elastography – 85.1% and FibroTest – 77%. There were no significant statistical differences between FibroTest-point elastography ($p = 0.85$), FibroTest-2D-SWE elastography ($p = 0.24$), TE-point elastography ($p = 0.06$), TE- 2D-SWE elastography ($p = 0.06$), point-2D-SWE elastography ($p = 0.42$) respectively. Significant statistical differences were found only between TE and FibroTest (94.6% vs 77%, $p = 0.0019$).

**Conclusion:** In this preliminary study, all ultrasound based elastographic methods had good performance for the diagnosis of compensated liver cirrhosis and this seem to be similar with FibroTest.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0005 LIVER-SPECIFIC SIRT1 DELETION AGGRAVATES HEPATIC FIBROSIS BY REGULATING BAS METABOLISM AND SUPPRESSES THE EXPRESSION OF IQGAP1

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**Introduction:** Hepatic fibrosis is a reversible wound-healing response characterized by the accumulation of extracellular matrix (ECM), in response to the stimulation of liver injury factors, hepatocytes damage and promote the activation of hepatic stellate cells. The of SIRT1 in the liver fibrosis remains poorly understood. Here, we demonstrate the influence and potential mechanisms of SIRT1 in murine liver fibrosis models.

**Aims & Methods:** Liver-specific SIRT1 deletion (SIRT1-LKO) mice and wild type (WT) mice were injected intraperitoneally (IP) 5 ml/kg body weight twice per week for 2 month with 10% CCL4 (dissolved in olive oil). Paraffin-embedded sections of liver tissue were stained with hematoxylin and eosin (H&E) and Masson's Trichrome staining to assess the collagen architecture and the extent of fibrosis. Serum ALT, bile acids concentrations were measured. We used label-free MS to screen differentially expressed proteins. Finally, we explored the potential mechanisms of SIRT1 in liver fibrosis in vitro.

**Results:** SIRT1-LKO mice treated with CCL4 showed more serious liver fibrosis compared with the WT mice according to H&E and Masson's Trichrome staining. Serum levels of ALT, AST were significantly higher in SIRT1-LKO mice than WT mice after CCl4 treatment, while BAs concentration was decreased. In CCl4-treated SIRT1-LKO mice, there was significantly higher expression of $\alpha$-SMA and Collagen 1A1. We analyzed the results of Label-Free mass spectrometry with a bioinformatics approach and discovered candidate gene-IQGAP1, CRABP1 and $\beta$-Catenin. Western blot and immunohistochemical staining were conducted to validate that SIRT1-LKO reduced the decreased expression of IQGAP1 compared with WT mice after treated with CCL4. However, SIRT1 and IQGAP1 were not shown to interact at exogenous level in SIRT1-overexpressing cells by coimmunoprecipitationin. Neither overexpression nor silence of SIRT1 affected the expression of IQGAP1 in L02 cells. These results indicated that SIRT1 influence the expression of IQGAP1 likely through indirect way. In LX2 cell, CDCA and DCA treatment increased IQGAP1 in a dose dependent manner.

**Conclusion:** We define a pivotal role of SIRT1 in liver fibrosis and explore the potential mechanism that SIRT1 prevents activation and proliferation of hepatic stellate cell by regulating bile acids metabolism in hepatocytes and influencing the expression of IQGAP1 in HSCs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0006 CONTRIBUTION OF THE TH17 IMMUNE RESPONSE TO THE PROGRESSION OF NON ALCOHOLIC FATTY LIVER DISEASE TO NON ALCOHOLIC STEATOHEPATITIS

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**Introduction:** Chronic inflammation is a key player in the progression from NAFLD to NASH. Morbid obesity is a known risk factor of NAFLD. It has been described that adipose tissue from obese patients has higher Th17 cell content than normal subjects. Th17 cells have been implicated in the pathogenesis of autoimmune and inflammatory diseases. The differentiation of naïve CD4 T cells into Th17 cells is triggered by TGF$\beta$, IL6 and IL1$\beta$, which induce the expression of their characteristic transcription factor Orphan Nuclear Receptor (RORC). After stimulation Th17 cells secrete IL-17 that binding its receptor IL-17RA, propagates a cascade of events that lead to neutrophil recruitment, inflammation and host defense. Periostin, one end-product of this pathway, is a secretory cell adhesion protein recently involved in pathogenesis of fibrosis observed both in vitro and in vivo.

**Aims & Methods:** The aim of the present study is to assess the Th17 immune response contribution to the progression of human NAFLD. Prospectively we included in the study 14 morbidly obese subjects undergoing bariatric surgery (7 men and 7 women with a mean age of 43 years (19–60), mean BMI 46.5). We analyzed mRNA expression of the Th17 pathway (RORC, IL-17, IL-17RA) and Periostin (POSTN) in liver and visceral adipose tissue biopsies. According to the histological assessment, patients were divided according Brunt's score of liver fibrosis F0 (n = 2), F1 (n = 5), F2 (n = 7). Data was correlated with the expression of other markers involved in inflammation (IL1$\beta$; TNF$\alpha$, VEGFA, IL8, IL6) and fibrosis (TGF$\beta$; $\alpha$SMA, COL1A1).

**Results:** We found that adipose tissue of patients with F2 stage of liver fibrosis shows an overexpression of RORC ($p < 0.05$) and IL-17RA ($p < 0.05$) genes respect to F0 group whereas IL17 was overexpressed only in F1 ($p < 0.001$). Moreover, hepatic gene expression of RORC ($p < 0.05$), IL17RA ($p < 0.05$) and Periostin ($p < 0.05$) was higher in the F1 and F2 group compared with the F0. No changes were observed in IL17 hepatic gene expression. All together these results are in line with those observed for inflammation IL1$\beta$; TNF$\alpha$, VEGFA, IL8 and fibrosis markers TGF$\beta$; $\alpha$SMA, COL1A1.

**Conclusion:** In obese patients, the Th17 pathway seems to be involved in the pathogenesis of liver inflammation and progression to fibrosis. Adipose tissue plays an important role as a source of IL17 conferring higher risk of NAFLD to these patients. Our preliminary data, in line with other reported studies, suggests that liver Periostin could be involved in hepatic fibrogenesis.

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## P0007 LIVER AND SKELETAL MUSCLE MIR-34A CONTRIBUTES TO MITOCHONDRIAL DYSFUNCTION AND INSULIN RESISTANCE IN EXPERIMENTAL NAFLD

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) pathogenesis associates with intracellular lipid accumulation and mitochondrial dysfunction in both the liver and skeletal muscle. In addition, we previously showed that, in human NAFLD progression, insulin resistance (IR) primarily targets the muscle although the liver is also affected. Still, the molecular mechanisms underlying the cross-talk between these organs during disease development remains poorly explored. Recent evidence supports a functional role for microRNAs (miRNA/miRs) in regulating NAFLD pathogenesis. In particular, activation of the miR-34a pro-apoptotic pathway correlates with NAFLD severity. Of note, miR-34a was recently described as a critical regulator of cardiomyocyte function, negatively impacting on cardiac repair and regeneration.

**Aims & Methods:** Our aims were to evaluate the potential role of miR-34a-dependent pathways in the development of mitochondrial dysfunction and IR in both muscle and liver cells in the context of NAFLD, using in vitro and in vivo disease models. C57BL6 mice were fed either a standard or a fast food (FF) diet for 25 weeks, or a methionine and choline-deficient (MCD) diet for 2 and 8 weeks. C2C12 muscle cells were incubated with or without palmitic acid (PA). Liver and skeletal muscle total RNA was used for miR-34a analysis by real-time RT-PCR. Protein levels of Sirtuin 1 (SIRT1), a key direct miR-34a target, mitofusion 2 (Mfn2) and peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1$\alpha$), two important players in mitochondrial dynamics and dysfunction, as well as endoplasmic reticulum stress-associated inositol-requiring enzyme 1$\alpha$ (IRE-1$\alpha$) were analyzed by Western Blot. IR was ascertained by assessing the activation/phosphorylation status of the insulin receptor / insulin receptor substrate 1 / Akt pathway.

**Results:** Mice fed the FF diet developed steatosis, inflammation and IR. MCD diet-fed mice developed steatohepatitis and severe liver damage and fibrosis. miR-34a expression levels were significantly increased in mice livers and skeletal muscle in both in vivo models, as compared with standard diet-fed mice ($p < 0.05$). Concomitantly, expression of SIRT1 was significantly decreased ($p < 0.05$). Further, in MCD-fed mice, expression levels of of PGC-1$\alpha$, which is also a transcriptional coactivator of SIRT1, as well as of mitochondrial fusion protein Mfn2 were significantly reduced ($p < 0.05$). Inversely, mitochondrial fission protein Drp1 and the unfolded protein response sensor IRE-1$\alpha$ were found increased ($p < 0.05$). Finally, incubation of C2C12 cells with PA activated the miR-34a/SIRT1 pro-apoptotic pathway, concomitantly with induction of cell death and IR, as well as reduced ATP levels ($p < 0.05$).

**Conclusion:** In conclusion, activation of the miR-34a/SIRT1 pathway in experimental NAFLD correlates with the development of IR and mitochondrial dysfunction in both liver and skeletal muscle. A better understanding of the overlapping roles of miR-34a in different tissues during NAFLD may help in establishing new therapeutic options (PTDC/BIM-MEC/0873/2012, UID/DTP/04138/2013, SFRH/BD/104160/2014, FCT, Portugal).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0008 INHIBITION OF CANONICAL WNT SIGNALING PATHWAY BY B-CATENIN/CBP INHIBITOR ICG001 AMELIORATES LIVER FIBROSIS IN VIVO THROUGH SUPPRESSION OF STROMAL CXCL12

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**Introduction:** Hepatic fibrosis, is a common pathological consequence of chronic liver diseases mainly caused by viral infections, alcohol abuse or metabolic syndrome leading to liver dysfunction, is the growing cause of mortality worldwide. In response to liver injury and altered wound healing response, quiescent hepatic stellate cells (HSCs) undergo characteristic morphological and functional changes and transform to proliferative, contractile and ECM-producing myofibroblasts.
**Aims & Methods:** In this study, we investigated implication of canonical Wnt signaling pathway in hepatic stellate cells and liver fibrogenesis. Activation of canonical Wnt signaling pathway was examined in vitro in activated HSCs (LX2), mouse 3T3 fibroblasts and in vivo in liver fibrosis mouse model. Effects of canonical WNT signaling pathway using $\beta$-catenin/CBP inhibitor ICG001 on fibrotic parameters and contractility were evaluated in TGF$\beta$-activated human HSCs and 3T3 fibroblasts. Effect on cell viability was examined at increasing concentrations of ICG001 using alamar blue assay. Finally, ICG001 was evaluated for efficacy in $CCl_4$-induced liver fibrogenesis mouse model.
**Results:** Canonical Wnt signaling pathway components (Wnt1, Wnt3a, Wnt 10b, FZD1, FZD2 and LRP5/6) were significantly up-regulated in TGF$\beta$-activated HSCs and 3T3 fibroblasts, and in vivo in liver fibrosis mouse model. In vitro, in TGF$\beta$-activated human LX2 cells and 3T3 fibroblasts, ICG001 significantly inhibited expression of major fibrotic parameters (Collagen I, $\alpha$-SMA, Vimentin, TIMP1 and PDGF$\beta$R) and 3D-collagen I gel contractility. No significant effects on cell viability was observed with increasing concentrations of ICG001. In vivo in $CCl_4$-induced acute liver injury mouse model, post-disease intraperitoneal administration of ICG001 (5 mg/kg) significantly attenuated collagen accumulation and HSC activation. Interestingly, ICG001 drastically inhibited macrophage infiltration, intrahepatic inflammation (IL-6, TNF$\alpha$ and CCL2 expression) and attenuated angiogenesis (CD34, CD31, SOX9 and VEGF expression). We further studied role of stromal factor SDF1/CXCL12 and observed complete inhibition of CXCL12 expression both in vitro and in vivo following Wnt inhibition suggesting potential role of CXCL12 in Wnt/b-catenin signaling during liver fibrogenesis. We therefore hypothesized that CXCL12 produced by activated HSCs (regulated by canonical Wnt signaling pathway) potentiates macrophage infiltration and activation leading to liver inflammation, and also promotes angiogenesis.
**Conclusion:** Because no effective treatment for liver fibrosis exists, pharmacological inhibition of Canonical Wnt signaling pathway thereby suppression of stromal factor CXCL12 suggests a potential therapeutic approach targeting activated hepatic stellate cells in liver fibrosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0009 HEPATITIS C CORE REGION MUTATIONS ARE CORRELATED WITH LIVER DISEASE PROGRESSION

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**Introduction:** Hepatitis C virus (HCV) core is a complex protein, capable of modifying HCV life cycle, participating in interactions with host proteins, altering cellular signalling pathways and contributing in hepatocarcinogenesis. HCV core region mutations were reported to be associated with advanced liver disease and increased risk of hepatocellular carcinoma.
**Aims & Methods:** The aim of this study was to determinate and compare HCV core region mutations in the serum and liver samples of the same patient at the time of diagnosis. The object was also to investigate the correlation of mutations determined at diagnosis and subsequent liver disease course. HCV RNA was isolated from serum and liver samples of 85 infected patients, collected at the time of diagnosis, at the Department of Gastroenterology, Clinical Hospital Center, Rijeka, Croatia. Viral RNA was transcribed to cDNA and the entire HCV core region was amplified using nested PCR. Amplicons were sequenced with Big Dye Termination v1.1. method on ABI 310 sequencer and compared with referent HCV genotypes from GenBank.
**Results:** Thirty patients were infected with HCV genotype 1 b, 29 patients with 1 a, 26 patients with 3 a. Thirteen patients demonstrated severe hepatitis activity grade, 44 patients moderate and 28 patients mild or minimal. Severe fibrosis stage was determined in 9 patients, moderate in 36 and mild or no fibrosis in 40 patients. Basal viremia above $1 \times 10^6$ IU/ml was determined in 32 patients and below $1 \times 10^6$ IU/ml in 53 patients. We determined identical core region sequence in serum and liver sample in 79 (93%) patients, confirming that serum is adequate material for analysis of viral parameters in chronic hepatitis C. Twenty-nine different core region missense mutations were identified in HCV genotype 1 a group, 106 in HCV genotype 1 b group and 61 in HCV genotype 3 a group. Missense mutations in the core region were determined in all 30 patients with genotype 1 b, ranging from one to nine mutations per patient. In contrary 17 (57%) patients in HCV genotype 1 a group, had no missense mutation in the entire core region. HCV genotype 1 b group represented majority of mutations. Of all 85 patients, 25 (34%) demonstrated more than 3 missense mutations in the core region of the same sample. 19/25 (76%) patients had severe or moderate hepatitis activity grade and demonstrated severe or moderate fibrosis. Genotype 1 b was determined in 13/25 (52%) patients with more than 3 missense mutations. The most frequent missense mutations identified were R70Q, T75A, M91L/C and A147V. R70Q, T75A and M91L were already reported as mutations promoting hepatocarcinogenesis and associated with increased HCC risk. Results of this study indicate significant correlation of HCV genotype 1 b and high basal viremia with presence of R70Q ($p = 2.831 \times 10^{-5}$; $p = 0.0202$), T75A ($p = 1.99 \times 10^{-12}$; $p = 4.384 \times 10^{-5}$) and M91L/C ($p = 1.169 \times 10^{-6}$; $p = 0.0902$) core region mutations. Progressive patohistological liver parameters (severe or moderate hepatitis activity grade and severe or moderate fibrosis stage) were associated with the presence of R70Q ($p = 0.0049$; $p = 0.0018$) and M91L/C ($p = 0.0413$; $p = 0.0223$) mutations.
**Conclusion:** Results of our study confirm that serum is adequate material for chronic hepatitis C viral parameters analysis. The frequency and the type of missense mutations positively correlate with liver disease progressivity. Core region missense mutations found at the time of diagnosis could serve as a prognostic parameter for liver disease subsequent course and patient outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0010 HIGH LEVELS OF SERUM AUGMENTER OF LIVER REGENERATION (ALR) PREDICT BETTER PROGNOSIS OF ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) AND ALR PROMOTER REGION GENETIC VARIANTS ASSOCIATE WITH ACLF RISK

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**Introduction:** Acute-on-chronic liver failure (ACLF) is a newly formed clinical entity characterized by acute decompensation of cirrhosis, liver failure, and a high mortality risk. Although it is know that both, acute and chronic hepatic insults could result in ACLF and hepatitis B virus infection and continuous alcohol intake damage the liver and induce ACLF, the defined risk factors have not yet been fully clarified. Clinical management of ACLF includes antiviral treatment, liver transplantation, liver dialysis, and replacement therapy according to the recommendations by the Asian Pacific Association for the Study of the Liver (APASL).
**Aims & Methods:** This study investigated serum augmenter of liver regeneration (ALR) levels' association with prognosis of hepatitis B virus (HBV)-related acute-on-chronic liver failure (ACLF). Then, the association of ALR single nucleotide polymorphisms (SNPs) with risk of HBV-related ACLF was assessed.
**Results:** A total of 100 ACLF, 100 mild-to-moderate chronic hepatitis B (CHB) infection, 100 liver cirrhosis (LC), and 100 hepatocellular carcinoma (HCC), and 100 healthy donors were enrolled. Serum ALR levels were detected using ELISA and 19 ALR promoter region SNPs were genotyped using PCR. The association between SNPs and ACLF risk was analyzed by the logistic regression model.
**Conclusion:** Serum ALR levels were $2.58 \pm 1.67$, $0.68 \pm 0.24$, $1.53 \pm 0.97$, $1.74 \pm 1.29$, and $0.72 \pm 0.29$ in ACLF, CHB, LC, HCC, and NC, respectively ($F = 7.028$, $P < 0.01$). Compared to healthy control, ACLF and HCC patients had dramatically elevated levels of serum ALR ($P < 0.01$ and $P = 0.035$, respectively). High levels of serum ALR predicted a better ACLF prognosis (OR, 6.4; 95% CI, 2.126–19.585; $P < 0.001$). Furthermore, four of the 19 ALR promoter region SNPs (G-721A, T-1199C, C-559A, and T-1285C) were associated with risk of developing ACLF ($P < 0.05$). However, none of these 19 SNPs was associated with serum ALR levels in ACLF patients ($P > 0.05$).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0011 THE ROLE OF SARTANS (TELMISARTAN OR OLMESARTAN) IN DECREASE OF INTERLEUKIN-6 LEVEL IN PATIENTS WITH STEATOHEPATITIS COMBINED WITH ARTERIAL HYPERTENSION AND OBESITY

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is one of the most widely spread chronic liver diseases of non-viral and non-alcoholic etiology. In recent years, a steady increase in the incidence of non-alcoholic steatohepatitis, which ranks 2nd among chronic liver diseases, is seen. In 14–20% of cases, NAFLD is combined with cardiovascular pathology, in particular – with arterial hypertension and coronary heart disease. An important role in the progression of these comorbid conditions is played by cytokines, especially interleukin-6. This pro-inflammatory cytokine stimulates the hepatic lipogenesis and is associated with obesity and insulin resistance.
**Aims & Methods:** The aim of the study was to assess the dynamics of interleukin-6 level and lipid spectrum of the blood in patients with steatohepatitis combined with arterial hypertension and obesity during administration of olmesartan or telmisartan in complex treatment with atorvastatin. The study enrolled 44 patients with steatohepatitis combined with arterial hypertension and obesity. Women and men were of equal average age – $55.6 \pm 1.5$. After initial tests for blood lipid spectrum and interleukin-6 level, all patients were divided into 2 groups. Throughout 12 weeks, the patients received sartans in standard dosages: 1st group – telmisartan, 2nd – olmesartan. In both groups, treatment was combined with atorvastatin.
**Results:** The therapy was effective in 17 (77.3%) patients in the 1st group and in 13 (59%) patients of 2nd group. Comparison of IL-6 levels in patients, who received both telmisartan and olmesartan, revealed a significant decrease of IL-6 level ($p < 0.001$). In addition, the study showed that 12 week-long administration of olmesartan or telmisartan in complex treatment with atorvastatin resulted in a significant decrease in levels of total cholesterol ($p < 0.01$) and LDL cholesterol ($p < 0.05$). At the same time, there was no significant difference in the levels of triglycerides and HDL cholesterol ($p > 0.05$).
**Conclusion:** Administration of olmesartan or telmisartan in complex treatment with atorvastatin in patients with steatohepatitis combined with arterial hypertension and obesity leads to inhibition of inflammatory responses which follow the course steatohepatitis. This is proven by the significant decrease of interleukin-6 level in both groups of patients ($p < 0.001$). In addition, the given combination of drugs significantly improves lipid metabolism by reducing the levels of total cholesterol ($p < 0.01$) and LDL cholesterol ($p < 0.05$).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0012 BACTERIAL ENDOTOXIN SIGNIFICANTLY DETERIORATE CONSEQUENCES OF EXPERIMENTAL LIVER INJURY THROUGH "EXPLOSION" OF CYTOKINES

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**Introduction:** Liver injury causes extensive immunological pro-inflammatory response characterized by significant growth of IL-1$\beta$, TNF$\alpha$, IL-6 and other pro-inflammatory mediators. Gram-negative bacteria infection exposes immune cells to lipopolysaccharide (LPS) from the bacterial cell membrane that induces a rapid cytokine response, which is essential for the activation of host defences against the invading pathogens. Following idea that microbial endotoxins cause similar immune reactions to liver injury we hypothesize that these effects may combine and/or even multiply.
**Aims & Methods:** The aim of this study is to determine the aetiology role for inflammatory/immunologic changes following liver injury emphasizing bacterial endotoxin as an experimental background for treatment corrections. Liver injury was modelled experimentally in 87 Wistar rats under general anaesthesia; sutures were applied immediately. Forty-five rats (51.72%) additionally received *S.typhimurium* endotoxin intraperitoneally. Twenty healthy rats formed control. Liquid chromatography and ELISA were used for determination of cytokines (TNF-$\alpha$, TGF-$\beta$1, IL-1$\beta$, and $\gamma$-INF) levels in liver tissue homogenates taken 24 hrs after injury.
**Results:** Aseptic liver injury alone cause minor changes in cytokines levels in liver homogenates compared to control: IL-1$\beta$ grew insignificantly ($55.72 \pm 8.30$ pg/g of homogenated hepatic tissue under liver injury compared to $45.37 \pm 5.82$ pg/g in healthy control rats, $p > 0.05$); TNF-$\alpha$ – $39.26 \pm 4.89$ pg/g and $47.63 \pm 6.47$ pg/g, $p > 0.05$, respectively; gamma-interferon ($\gamma$-INF) – $112.9 \pm 7.62$ pg/g and $123.9 \pm 10.75$ pg/g, $p > 0.05$; TGF-$\beta$1 – $204.5 \pm 12.17$ pg/g and $196.2 \pm 6.42$ pg/g, $p = 0.06$. Endotoxin added intraperitoneally caused explosive growth of cytokines in liver tissue homogenates: IL-1$\beta$ increased over 80% to $74.27 \pm 8.09$ pg/g, $p < 0.01$; TNF-$\alpha$ grew 45% to $56.91 \pm 6.53$ pg/g, $p < 0.05$; $\gamma$-INF level ($419.16 \pm 30.68$ pg/g) raised 3.7 times compared to liver injury without endotoxin, $p < 0.001$. In contrast, TGF-$\beta$1 remained almost unchanged – $236.16 \pm 25.68$ pg/g, $p > 0.05$.
**Conclusion:** Although liver injury is generally accompanied by pro-inflammatory tendencies, though they are generally insignificant in case of isolated aseptic and immediately cured trauma. However, this presents the ideal, theoretic condition; raised endotoxin level is inevitable in case of real clinical situation related to acute trauma or chronic liver disease. Changes of microbiome and rapid release of endotoxin play an even more important role than the liver injury itself, which rather acts as a trigger factor. Obtained data shows that better control of microbial lipopolysaccharide-endotoxin influence must be ensured in order to achieve sufficient results and prevent further liver inflammation. This may be valid for not only trauma itself but also any liver injury including surgery and possibly autoimmune disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0013 FUNGAL INFECTIONS IN CIRRHOTIC PATIENTS – MARKER FOR AN ADVERSE OUTCOME?

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**Introduction:** Liver cirrhosis is increasingly being considered a state of immunosuppression and sepsis is nowadays seen as a major threat for these patients. Due to increased use of broad-spectrum antibiotics, particularly for the prophylaxis of spontaneous bacterial peritonitis, fungal infections are a growing concern in Hepatology.
**Aims & Methods:** Our objective was to evaluate the impact of fungal infections on the prognosis of decompensated cirrhotic patients. Two groups of decompensated cirrhotic patients were compared (2010–2014). Group A included patients with a documented fungal infection. Group B patients had no evidence of fungal infection. Clinical, biochemical and microbiological data was collected. Short and long-term prognosis of the two groups was compared.
**Results:** A total of 86 patients were included (Group A–34; Group B–52). In both groups, there was a predominance of male patients (Group A–70.6%; B–90.4%), with similar average age (A-$64.8 \pm 8.3$; B-$63.2 \pm 7.8$ years-old). Group B patients had more severe liver disease, as 76% were classified as Child-Pugh Class C vs 41.2% in group A ($p < 0.0001$); average MELD score was also higher in group B (16.9 vs 18.7; $p > 0.05$). Patients with fungal infections (Group A) had a significant longer length of stay (LOS) – 22.6 vs 10.2 days ($p < 0.001$). The mortality rate as inpatients and in the 3 months following discharge was also much higher in group A (inpatient mortality: 52.9% vs 4%, $p < 0.0001$; 3 month mortality: 29.4% vs 9.6%, $p = 0.0001$).
Further analysis of group B revealed that admission was mainly due to portosystemic encephalopathy (23%), followed by spontaneous bacterial peritonitis (17.6%) and urinary sepsis (17%). Fungal infections were caused by *Candida albicans* in 64.7%, while other Candida species were responsible for the remaining cases. About two-thirds involved the urinary tract. Fluconazol and Anidulafungin were the preferred antifungal agents (70.6% and 18.5%, respectively). The average number of antibiotics used before the diagnosis of fungal infection was 1.5 (0–4).
**Conclusion:** In our study, fungal infections were undoubtedly associated with an adverse outcome, with longer LOS and significantly higher mortality rates, despite occurring in patients with less severe liver disease. In decompensated cirrhotic patients, especially if exposed to broad-spectrum antibiotics, careful search for fungal infections and appropriate treatment should be systematically adopted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0014 GUT MICROBIOTA SIGNATURES IN TURKISH NAFLD PATIENTS.

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**Introduction:** The bacterial overgrowth in the intestine, disruption of the balance in the gut microbiota (dysbiosis) may have an effect on NAFLD pathogenesis. The purpose of the present study is to compare the gut microbiota of the patients with NAFLD and the healthy controls by quantitative Real Time PCR (qPCR) analysis. Gut microbiota is affected by environmental and specific dietary patterns. This is the first study in Turkish NAFLD patients with diverse cultural dietetic habits. In order to understand the potential role of gut dysbiosis and subsequent translocation of bacterial products, serum endotoxin levels were also analyzed.
**Aims & Methods:** The stool and serum samples from 52 NAFLD patients and 38 healthy controls have been collected. qPCR analysis of *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, *Lactobacillus spp.*, *Bifidobacterium spp.*, *Bacteroides fragilis* group was performed. Serum endotoxin levels were also determined by Chromogenic LAL Assay. Dietary habits were analysed by nutritional questionnairs.
**Results:** *Akkermansia muciniphila* and *Bacteroides fragilis* group were significantly lower in patients with NAFLD as compared with the healthy control ($p < 0.001$). No significant difference was determined in terms of *Lactobacillus spp.*, *Bifidobacterium spp.* and *Faecalibacterium prausnitzii* counts. Moreover, significantly elevated endotoxin levels were determined in NAFLD patients (9.04 EU/mL in NAFLD group; 2.75 EU/mL in control group; $p < 0.05$).
**Conclusion:** *Akkermansia muciniphila* and *Bacteroides fragilis* group has been known to have beneficial effects on gut barrier function. These two bacterial groups were decreased in Turkish NAFLD patients. Decreased levels of these bacteria were also shown in metabolic syndrome, which is frequently associated with NAFLD. NAFLD patients have also increased endotoxin levels which indicate a translocation of bacterial products as a result of increased gut permeability.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0015 RETROSPECTIVE ANALYSIS OF THE MICROBIAL EPIDEMIOLOGY OF SPONTANEOUS BACTERIAL PERITONITIS AND BACTERIASCITES IN PATIENTS WITH LIVER CIRRHOSIS

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**Introduction:** Current guidelindes recommend the use of 3rd generation cephalosporines for antibiotic therapy of spontaneous bacterial peritonitis (SBP). Response rates to this therapy are reported with 76–98%. Bacterial translocation of grampositive bacteria including enterococcae and specific local resistance patterns may result in inferior response rates to 3rd generation cephalosporines. Knowledge on local microbial epidemiology privides evidence to optimize antibiotic therapy.
**Aims & Methods:** Microbial epidemiology of ascitic fluid cultures and resistance patterns obtained from patients with liver cirrhosis between 2013–2015 at a tertiary care center (Krankenanstalt Rudolfstifung, Vienna) were retrospectively analyzed.
**Results:** In total 482 ascites cultures of 200 cirrhotic patients were analyzed. Median age was 62.2 (31.2–91.8) years, the majority (73%, M:146/F:54) were men, and the main etiology was alcoholic liver disease (83% ALD), followed by viral hepatitis (8.9%), autoimmunie (0.8%), and cryptogenic (7.3%). Thirty-one (6.4%) of ascitic fluid cultures reveiled positive results, and 12.5% of all patients (25/200) had at least one positive culture result. While 17 (3.5%) of patients had bacteriascites, 58 (12%) of patients had SBP – among those 47 (81%) had no germ isolated at their asicitic fluid culture. The most common species were *Streptococcus spp.* (n = 7/22.6%) followed by *Candida spp.* (n = 6/19.4%), *E. coli* and *Staphylococci* (n = 5/16.1%) and *Enterococci* (n = 3/9.7%). 28% of all bacteria were resistant towards aminopenicillines/betalactamase-inhibitors. There was a resistance rate of 18.5% of all germs towards 3rd generation cephalosporines.
**Conclusion:** Considering the local microbial epidemiology, the initial empirical antibiotic treatment for SBP should have good efficacy from grampositive bacteria including Enterococci. The recommendation for empiric antibiotic therapy of patients with liver cirrhosis with inherent immunosuppression should be adapted according to local resistance rates.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0016 THE ADAPTOR PROTEINS CARDIF/STING NEGATIVELY REGULATE THE PROLIFERATION OF LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

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**Introduction:** The innate immune system is of crucial importance for the regulation of liver regeneration. Nucleic acid sensors are know to play a major role within this context, however, there is only limited knowledge on the role of central adaptor proteins, such as CARDIF and STING, during liver regeneration. The aim of the present study was to analyze CARDIF and STING during liver regeneration. Our hypothesis states that these known modulators of the innate immune system have an influence on liver regeneration by direct activation of CARDIF/STING-dependent cytosolic sensors.
**Aims & Methods:** In order to examine the influence of these two proteins on liver regeneration, we use a newly established CARDIF/STING knockout mouse model and compared it to a C57BL/6 mice control cohort. A 2/3 partial hepatectomy (PH) was performed in both groups and mice were analyzed at eight designated timepoints after surgery (n = 80 mice in total). Liver regeneration was quantified by liver-to-body weight ratio, while proliferation was determined by BrdU staining. Additionally, RNA- and protein levels of proliferation markers were analyzed in resected tissues while pro-inflammatory cytokines were measured in murine serum.
**Results:** CARDIF/STING knockout mice showed a significantly impaired liver regeneration after PH. Additionally, we detected a strong difference in BrdU staining at several time points after PH underlining an inhibition of proliferation in the absence of CARDIF and STING. Expression analysis of Interleukin-6 (IL-6) revealed a significant decrease in the wild type cohort after PH. In addition, the membrane-bound form of the IL-6 receptor was found to be increased in the control group 2, 4 and 8 h after PH, while the soluble form of the receptor was significantly increased 12 h post-PH. In CARDIF/STING knockout mice, the proliferation marker Cyclin D1 was decreased until 24 hours after surgery, while $p21^{Cip1}$ expression, which is associated with a cell cycle arrest, was increased 8 h post-PH.
**Conclusion:** Together, these data provide the first experimental evidence that CARDIF/STING knockout mice show a delayed liver regeneration. These data support the concept that CARDIF and STING play a major role in liver regeneration during physiological conditions. In the absence of these two proteins, we observed a modulated immune response which lead to a negative regulation of the proliferative capacity in liver after partial hepatectomy. This finding could impact on the future development of molecular therapies making use of the innate immune system.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0017 THE ROLE OF GENETICALLY MODIFIED HSCS IN LIVER REGENERATION AFTER ACUTE LIVER DAMAGE

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**Introduction:** Actual problem of modern hepatology is to find a new treatment for liver diseases. Nowadays gene and cell therapy methods using hepatic stellate cells (HSCs) that are thought to be regional stem cells of the liver, are considered as a new perspective approach. It is assumed that using genetically modified cells that express and overexpress therapeutic factors, could reduce the therapeutic dose of transplanted cells and enhance therapeutic effects of these cells. However, it remains unclear, the influence of genetically modified cells, in this case HSCs, on liver regeneration and therapeutic effects of these cells after transplantation into the organism.
**Aims & Methods:** We aimed to study the role of genetically modified HSCs (by using the adenoviral vector Ad5-optHGF-optFGF4-RFP) on liver regeneration after transplantation into the rats with acute liver damage. Genetic modification of HSC was carried out by using adenoviral vector Ad5-optHGF-optFGF4-RFP, which contains hepatocyte growth factor (HGF), fibroblast growth factor-4 (FGF-4), and red fluorescent protein (RFP). We selected the classical model of acute liver damage – partial hepatectomy (PH). Genetically modified HSC were injected into portal vein during the PH operation. Control group of animals have received the same cells without PH operation. The animals were sacrificed after 1, 2, 3, 5, 7, 14, 28 days after the transplantation of HSC. Paraffin slices were stained by immunohistochemistry with antibodies to RFP, desmin – marker of HSC and a-SMA – myofibroblast marker.
**Results:** RFP + cells were detected in parenchyma in both groups even at first days after transplantation. They varied in shape and location in the liver in different days of experiment. Small oval-shaped RFP + cells were stained from the first day near the portal tracts. At the same time hepatocyte-like RFP + cells were also found here from the first day. Maximal number of such cells was found on the 5th day after transplantation in both groups, but in the experimental group average number of cells was higher than in control. Coincidently, the intensity

and quickness of hepatocyte repopulation in liver were higher in the group of animal after PH. Number of desmin + cells increased more in the experimental group comparing with the control one. In both groups a-SMA-positive cells were not detected.
**Conclusion:** Genetically modified HSCs, which is transduced by HGF and FGF-4 genes, save their viability after transplantation into the rat after PH, migrate and integrate into the liver parenchyma. These cells have a positive influence on the process of liver regeneration without the risk of liver fibrosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0018 ANGIOTENSIN II TYPE 1 RECEPTOR GENE A1166C POLYMORPHISM IS ASSOCIATED WIT NON ALCOHOLIC FATTY LIVER DISEASE AND PREDICTS ITS SEVERITY

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**Introduction:** The pathogenesis of non alcoholic fatty liver disease (NAFLD) has not been well demonstrated yet, however, genetic predisposition is probably of major importance. Angiotensin II type I receptor (AGTR1) have been known to be involved in the process of liver fibrosis and metabolic syndrome.
**Aims & Methods:** This study aimed to investigate the association between AGTR1 A1166C polymorphism and NAFLD. A cross-sectional study was conducted between March 2014 and March 2015 among healthy adult individuals referred to our radiology clinic for abdominal ultrasonography. NAFLD was diagnosed by an expert radiologist based on the presence of these ultrasonographic findings: hepatorenal echo contrast, liver brightness, deep attenuation, vascular blurring and the absence of hepatitis B surface antigen or antibody to hepatitis C virus, 2) alcohol consumption (>20 g/day), 3) history of other causes of liver disease, and 4) medications known to produce fatty liver disease during the last six months prior to the study. Participants' characteristics and their lab data including liver function tests, lipid profile, fasting plasma glucose (FPG) were also recorded. AGTR1 A1166C polymorphism was checked in subjects with NAFLD and healthy controls using TaqMan allelic discrimination method.
**Results:** Fifty eight subjects with NAFLD were compared with 88 individuals without NAFLD. Mean of all anthropometric indices including BMI, weight, height, waist circumference and hip circumference were significantly higher in subjects with NAFLD compared to those without NAFLD ($P < 0.05$). Mean total cholesterol was significantly higher in subjects with NAFLD in comparison to the controls in univariate analysis ($P = 0.018$). Higher serum ALT was also a predictor of NAFLD ($38.56 \pm 17.61$ versus$20.76 \pm 6.40$ IU/L) ($P = 0.0001$). Metabolic syndrome was detected in 31 (53.44%) individuals in NAFLD group and in 27 (19.01%) in control group ($P < 0.001$) (OR: 3.51, 95% CI: 1.84–6.66). Multivariate logistic regression analysis of risk factors showed that body mass index (BMI), metabolic syndrome, waist circumference, hip circumference and serum ALT were independent predictors of NAFLD in our study population. The frequency of AA and CC genotypes of AGTR1 gene was significantly higher in patients with NAFLD compared to controls ($P = 0.029$ and $P = 0.042$ respectively). Furthermore, C allele was more detected in subjects with NAFLD compared to healthy controls (OR: 2.1; 95% CI: 1.23–3.61, P-Value = 0.006). CC genotype (OR: 10.62; 95 %CI: 1.05–106.57, P-Value: 0.045) and C allele (OR: 6.81; 95 %CI: 1.42- 32.48, P-Value: 0.016) were also predictors of severe fatty liver disease in our study population.
**Conclusion:** Our results provide the first evidence that AGTR1 gene A1166C polymorphism not only is associated with NAFLD and but also may predict its severity. Multivariate regression analysis for the NAFLD predictors.

| | OR | (95% CI) | P-value |
|---|---|---|---|
| Body mass index (BMI) | 7.74 | (1.25-3.73) | 0.005 |
| Waist circumference | 9.26 | (0.68–0.92) | 0.002 |
| Hip circumference | 5.21 | (1.02–1.39) | 0.022 |
| Metabolic syndrome | 15.21 | (9.74–14.43) | <0.001 |
| Alanine aminotransferase (ALT) | 26.46 | (1.19–1.50) | <0.001 |

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0019 PATIENTS WITH POLYCYSTIC LIVERS MORE THAN TWO TIMES THE NORMAL SIZE ARE LIKELY TO DEVELOP SYMPTOMS

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**Introduction:** Progressive growth of hepatic cysts can lead to symptomatic hepatomegaly in polycystic liver disease (PLD).
**Aims & Methods:** Our primary aim was to determine at which threshold of liver volume PLD patients become symptomatic. As a secondary objective we investigated which symptoms are associated with higher liver volume. We used the PLD questionnaire (PLD-Q), a validated questionnaire that assesses frequency and discomfort of PLD-related symptoms, to determine the symptom burden. In a cohort of 291 PLD patients that have completed the PLD-Q and rated themselves as symptomatic or not (NCT02173080), we have defined the PLD-Q cut-off value of being symptomatic with receiver operating characteristic (ROC) analysis. The optimal PLD-Q cut-off score was 31 points with an area under the curve (AUC) of 0.832 ($p < 0.001$). Next, we used baseline data of PLD patients from two prospective studies (DIPAK observational study and CURSOR randomized controlled trial (NCT02021110). All patients completed the PLD-Q and had liver volume imaging (CT or MRI) measured by segmentation. In order to determine the liver volume cut-off value for being symptomatic, we used the PLD-Q cut-off value from the previous step in another ROC analysis with liver volume as independent variable. Spearman correlations were calculated between symptoms and liver volume.
**Results:** We included 82 of the 131 patients from the prospective studies (main exclusions: no PLD n = 26, no PLD-Q n = 7 or no imaging n = 8). Most patients were female (n = 67) with a mean age of 48 years. Median liver volume was 3879 mL (IQR: 2452 – 5891). Cut-off liver volume for being symptomatic was 3472 mL (AUC 0.805, $p < 0.001$) with a sensitivity of 80% and a specificity of 73%. This cut-off volume has a positive and negative predictive value of 66% and 82% respectively. Dissatisfaction with abdomen size was strongly correlated with liver volume (r = 0.63). Fullness, early satiety, pain in rib cage, shortness of breath, limited mobility, anxiety about the future and, problems with intercourse correlated moderately (r = 0.40–0.59). There was a weak correlation with lack of appetite, pain in side and tiredness (r = 0.20–0.39). Nausea (r = 0.17, p = 0.146) and abdominal pain (r = 0.17, p = 0.127) were not correlated with liver volume.
**Conclusion:** Patients with liver volumes equivalent to two times the normal size are likely to develop PLD-related symptoms. In patients with smaller livers, other causes that lead to similar symptoms should be considered. Most PLD-related symptoms are associated with larger liver volume, except for nausea and abdominal pain.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0020 LNCRNA PROFILE IN NAFLD AND IDENTIFICATION OF A PROTECTIVE NOVAL LNCRNA FLRL2 IN NAFLD

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent chronic liver diseases worldwide with unclear mechanism. Long noncoding RNAs (lncRNAs) have recently emerged as important regulatory molecules in liver diseases.
**Aims & Methods:** To further understand the pathogenesis of NAFLD, lncRNA and mRNA microarray was conducted in NAFLD mice model. Potential target genes of significantly changed lncRNA were predicted using cis/trans-regulatory algorithms, followed by Gene Ontology analysis and KEGG pathway enrichment analysis. NAFLD mice model and NAFLD AML12 cell model were used in further experiments. Real-time qPCR and Western Blot were adopted in effect test after manipulations with certain siRNA or shRNA transfection. Oil Red O/ HE staining and total triglyceroil kit were applicated in celllular steatosis evaluation. Dual luciferase assay was used in identifying promoter activity of certain genes.
**Results:** In current analysis, 89 up-regulated and 177 down-regulated mRNAs were identified, together with 291 dysregulated lncRNAs. Bioinformatic analysis of these RNAs has categorized these RNAs into pathways including arachidonic acid metabolism, circadian rhythm, linoleic acid metabolism, Peroxisome Proliferator Activated Receptor signaling pathway, sphingolipid metabolism, steroid biosynthesis, tryptophan metabolism and tyrosine metabolism were compromised. Quantative PCR of 9 mRNAs and 8 lncRNAs of interest (named as fatty liver related lncRNA, FLRL) was conducted and verified previous microarray results. Several lncRNAs, such as FLRL1, FLRL6 and FLRL2 demonstrated to be likely a key player in circadian rhythm targeting Per3, Per2 and Arntl. While FLRL8, FLRL3 and FLRL7 showed their potential role in PPAR signaling pathway through interaction with Fabp5, Lpl and Fads2. Mechanism of FLRL2 as well as its potential target circadian rhythm gene Arntl was investigated. Western blot and qPCR both revealed a decreased trend of FLRL2 as well as Arntl in NAFLD in vivo, in vitro models. Overexpression of FLRL2 reverses lipid accumulation, ER stress and lipogenesis, which are main

pathophtsiological changes in NAFLD. In the mean while, shRNA knock down of FLRL2 lead to excerbation caused by FFA treatment, a classical NAFLD cell model. Bioinformatic analysis pointed to potential cis-interaction of FLRL2 and Arntl gene. Both knock-down or knock in of FLRL2 caused possitive feedback of Arntl expression. As a clock protein, Arntl has been identified to be a Sirt1-regulator through transcriptoin level. Dual luciferase assay has proved interaction between Arntl and Sirt1 gene promoter, which was inhibited in NAFLD cellular model and rescued by Arntl overexpression. Similar with FLRL2, inhibition of Arntl led to NAFLD excerbation, while overexpression played a protective role, measured by ER stress, lipid accumulation and over-lipogenesis.
**Conclusion:** This is the first study focusing on NAFLD lncRNA profile in rodent model and also first time in identification of NAFLD-related FLRL2 as well as mechanism exploration. We characterized global changes in lncRNAs and mRNA in NAFLD. 89 up-regulated and 177 down-regulated mRNA were identified, and 291 dysregulated lncRNAs, with 111 increased and 180 decreased were discovered. Function of these changes hasn't be fully elucidated, but potential pathways involved were predicted, such as arachidonic acid metabolism, circadian rhythm, linoleic acid metabolism, PPAR signaling pathway, sphingolipid metabolism, steroid biosynthesis, tryptophan metabolism, tyrosine metabolism. Among all changed lncRNAs, FLRL2 showed potential role in NAFLD pathogenesis through Arntl-Sirt1 axis. Current study provided new insight into pathogenesis of NAFLD, involving lncRNAs. Further study will focus on the molecular mechanism of these changes as well as interacting pattern of FLRL2 and Arntl.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0021 NON-ALCOHOLIC FATTY LIVER DISEASE ASSOCIATED WITH METABOLIC SYNDROME: MAJOR RISK FOR ATHEROSCLEROSIS

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) affects about 1 billion people worldwide. Those with non-alcoholic steatohepatitis (NASH) have increased mortality rates compared to the general population. Cardiovascular diseases are the leading cause of death in NASH patients. Identifying those which are at higher risk for developing cardiovascular events is of major importance, both in terms of prognosis, as in the terms of therapeutic attitude.
**Aims & Methods:** Our aim was to identify those patients which are at higher risk for developing cardiovascular events, by quantifying subclinical atherosclerosis in patients with NAFLD and MS. Through this, we tried to identify a screening strategy for cardiovascular disease and to identify an optimal moment for initiating therapeutic intervention. We included patients with NAFLD and metabolic syndrome (MS), which we divided into 4 arms: patients with NAFLD and with MS, patients with NAFLD without MS, patients with MS without NAFLD and controls. We performed ultrasound measurement of the carotid intima-media thickness (common carotid artery, 1 cm before the bifurcation). Values above 0.06 were considered increased. Values above 0.12 cm were considered as atherosclerotic plaques. We used Fibromax for evaluating NAFLD severity (presence of NASH, degree of fibrosis and steatosis). We performed liver enzymes determination, lipid profile, glycaemic profile and antropometric measurements. We determined the levels of IL-6, IL-18, adiponectine and leptine. For statistical analyses we performed chi-squared test, Fisher exact test, Kruskal-Wallis and Mann-Whitney tests, ANOVA test, Spearman's rank correlation coefficient using R Foundation for Statistical Computing, IBM SPSS v.19 and Statistics v.6.0.
**Results:** We included 157 patients in all 4 arms, with no significant differences regarding the age ($F(3.153) = 2.74$, $p = 0.05$) and sex ($\chi2(1) = 2.99$, $p = 0.392$). Patients with NAFLD and MS had intima-media thickness values greater than those with NAFLD without MS ($U = 708.5$, $p = 0.002$) and greater than controls ($U = 498$, $p < 0.001$). Between intima-media thickness values in those with isolated MS and in those with NAFLD with MS, no significant differences were found ($U = 407.5$, $p = 0.21$). In all patients with NAFLD, with and without MS, there was a correlation between the value of intima-media thickness and the presence of NASH ($U = 225$, $p = 0.025$), the degree of steatosis ($\rho = 0.296$, $p = 0.027$) and the degree of fibrosis ($\rho = 0.466$, $p < 0.001$). We identified in all patients with NAFLD, with and without MS, a positive monotonous correlation between the degree of steatosis and leptin ($\rho = 0.3$, $p = 0.025 < 0.05$). These levels of leptin were higher in those with more severe steatosis. Also in this group of patients we identified a good positive correlation between the interleukin 18 and the presence of NASH ($\rho = 0.701$, $p < 0.001$). Those with NASH had higher values of interleukin 18. The presence of atherosclerotic plaque has been influenced by the the degree of fibrosis ($U = 131$, $p < 0.001$). The sex of the patients ($\chi2(1) = 0.30$, $p = 0.638$) and the level of total cholesterol ($U = 738$, $p = 0.438$), LDL-cholesterol ($t(91) = 0.67$, $p = 0.505$), HDL-cholesterol ($t(93) = 0.75$, $p = 0.458$), and triglycerides ($U = 803.500$, $p = 0.911$) did not affect the presence of atherosclerotic plaque, nor on the entire group of patients or on each arm. In the logistic model for the prediction of the risk for developing atherosclerotic plaque, the degree of fibrosis was a predictor with a positive effect on the presence of atherosclerotic plaque ($p = 0.004$, adjusted $OR = 7.19$).
**Conclusion:** The patient with NAFLD was found to be atypical for the development of cardiovascular risk. The association between NAFLD and MS predisposes to an increased cardiovascular risk. The development of MS in patients with NAFLD implies the acceleration of atherosclerosis and thus increasing the cardiovascular risk. The determination of leptin, interleukin 18, as well as performing ultrasound measuring of the carotid intima-media thickness may be useful to quantify the severity of liver disease. The characterization of the liver disease and, especially the grading of fibrosis, has proved to be an important prognostic factor for cardiovascular disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0022 CAUSES OF DEATH IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: RESULTS FROM A TERTIARY HOSPITAL IN SOUTH CHINA

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD), which would progress to cirrhosis and hepatocellular carcinoma, is the most rapidly increasing hepatic diseases worldwide and has become the leading cause of chronic liver disease in China. There is no published data related to NAFLD mortality from Chinese subjects.
**Aims & Methods:** This cross-sectional study was designed to analyze the causes of death and clinical characteristics among death cases with NAFLD in south China. The clinical information of patients who died during hospitalization in the First Affiliated Hospital of Sun Yat-sen University from January 2009 to December 2011 was collected from medical records. NAFLD was diagnosed only if fatty liver was confirmed by imaging examination, either by ultrasound, computed tomography or magnetic resonance imaging. Exclusion criteria included overdrinking and with other liver disease. ICD-10 death classification was used to investigate the cause of all deaths. Clinical and laboratory tests for patients were analyzed and compared with the other death cases without NAFLD.
**Results:** In total, 694 patients had available radiological data, including 102 (14.6%) of patients with NAFLD and 592 controls. Of NAFLD group, 70 (68.6%) were males and the median death age was $66.53 \pm 23.45$ years. The most frequent death cause was cardiocerebral vascular diseases (39.2%) followed by extrahepatic malignancy (32.3%) , infection (6.9%) and liver related disease (3.9%) . The percentage of patients died of cardiocerebral vascular diseases (39.2%) was significant higher in NAFLD group than that of controls (13.8%, $p = 0.027$), while the rate of NAFLD patients died of liver related disease (3.9%) showed obvious lower than that of controls (13.8%, $p = 0.005$) . According to whether death cause is cardiocerebral vascular diseases (CVD), NAFLD were divided into 2 subgroups, CVD group and non CVD group. CVD group had significantly higher total cholesterol levels ($6.43 \pm 0.63$ mmol/L vs $6.02 \pm 0.87$ mmol/L, respectively, $P = 0.011$) and higher triglyceride ($2.44 \pm 0.82$ mmol/L vs $2.05 \pm 0.76$ mmol/L, $P = 0.015$) and higher LDL- cholesterol ($3.79 \pm 0.43$ mmol/L vs $3.62 \pm 0.35$ mmol/L, $P = 0.031$) compared with non CVD group. There was no difference of body mass index, liver function, blood routine test, blood pressure, fasting serum glucose levels, serum uric acid levels, HDL-cholesterol levels among the two subgroups.
**Conclusion:** Cardiocerebral vascular disease is the predominant death cause in NAFLD participants. Cardiocerebral vascular diseases account for a higher proportion of death cause but liver-related diseases less in NAFLD patients than individuals without NAFLD. NAFLD patients who died of cardiocerebral vascular diseases may have more severe dyslipidemia than those of other death cause.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0023 THE EFFICACY AND SAFETY OF VILDAGLIPTIN TREATMENT FOR NONALCOHOLIC FATTY LIVER DISEASE IN TYPE 2 DIABETES MELLITUS

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**Introduction:** It is known that dipeptidyl peptidase-4 inhibitors were useful for the treatment of type 2 diabetes mellitus (DM). However, effects of these drugs on liver function and glucose metabolism in nonalcoholic fatty liver disease (NAFLD) have not been well determined. Except the improvement of glycemic control observed in type 2 DM; dipeptidyl peptidase IV (DPP-4) inhibitors have also been reported to have non-glycemic actions with decreasing receptor for advanced glycation end-products (RAGE) expression [1], vascular relaxation and increasing nitric oxide release [2] reducing lipid and protein oxidation [3] improving hepatic steatosis [4] or anti-inflammatory actions [5]. We evaluated the effect of vildagliptin on nonalcoholic fatty liver which has a widespread use in the treatment of diabetes.
**Aims & Methods:** The aim of this study was to evaluate the effect of vildagliptin on liver functions and hepatic steatosis and also to evaluate efficacy and safety of vildagliptin in NAFLD patients with type 2 DM.Fifty-four patients with Type 2 DM, whom were newly started vildagliptin treatment and diagnosed as NAFLD by ultrasonography, were prospectively enrolled from June 2014 to June 2015 in Bozok University Hospital, Yozgat, Turkey. All patients were subjected to lifestyle intervention of diet and physical exercise after the diagnosis of T2DM. Patients aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP), HbA1c,

waist circumference (WC), body mass index (BMI), triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and demographic characteristics were recorded before, 3 and 6 months after the initiation of treatment. Liver non-invasive assessment tools such as, Fatty Liver Index (FLI), FIB-4 score, APRI Score, were also evaluated. Vildaliptin treatment was given 100 mg per day.

**Results:** Characteristics of patients were given in Table 1 during and pretreatment time. HbA1c was reduced from $8.48 \pm 1.43\%$ to $7.87 \pm 1.35\%$ ($P < 0.001$). There were no significant difference between patients AST, GGT, ALP, HDL and FIB-4 score before and after treatment values ($P > 0.05$). HbA1c was reduced from 8.95% (8.07–10.35) to 7.00% (6.27–8.10) ($P < 0.001$). During vildagliptin treatment, ALT levels improved from $30.91 \pm 26.48$ to $25.94 \pm 14.8$ IU/L ($P = 0.048$). The serum levels of TG and LDL decreased with statistical significance ($P < 0.05$). WC and BMI were also decreased ($P < 0.001$). FLI and APRI score improved at 6 months after the initiation of vildagliptin. All the patients could take vildagliptin of 100 mg/day without reduction necessitated by related side-effects.

**Conclusion:** Our preliminary study results showed that vildagliptin treatment have positive effect on blood sugar regulation, body composition, ALT and non-invasive liver tools for the treatment of T2DM complicated with NAFLD. Our results indicated that vildagliptin is effective and safe in NAFLD patients with Type 2 DM.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0024 DIAGNOSTIC ALGORITHM FOR HIGH LIVER IRON OVERLOAD: RESULTS FROM A PROSPECTIVE STUDY OF 312 PATIENTS WITH HYPERFERRITINEMIA


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**Introduction:** Hyperferritinemia is a common finding in routine laboratory tests.

**Aims & Methods:** To develop and validate a diagnostic algorithm for high iron overload (HIO) based on laboratory and genetic variables.

We collected a retrospective cohort with all consecutive patients between 2001–2008 studied by Magnetic Resonance Imaging (MRI) to determine liver iron concentration (LIC). This cohort served as the derivation set. We analyzed all variables using univariate statistics with the MRI acting as the gold standard. We studied the best combination of the diagnostics variables to build the algorithm. We validated the algorithm in a prospective cohort, collecting all patients referred to our hospital for study of iron metabolism alteration between 2009–2013 (validation set). HIO is considered if the Hepatic iron index (LIC/age) > 1.9 (estimated by MRI).

**Results:** Retrospective cohort: 242 patients (198 men/44 women), mean age 52.4 (SD 13.3). Thirty six of them had HIO. Nearly half of the patients (117/242 = 48.4%) had both Transferrin saturation index (TSI) and Ferritin elevated and 28 (11.5%) were C282Y homozygous. The final algorithm was as follows: We consider a patient as having HIO with the simultaneous occurrence of TSI and Ferritin elevated and C282Y homozygosis. HIO is discarded if TSI or Ferritin are within normal values. The rest should be studied by MRI.

Prospective cohort: 312 patients (272 men/40 women), mean age 55 (SD 13.5). Mean ferritin 729.6 (SD 449.6), mean TSI 40.8 (SD 15.8).

The nosological characteristics of the algorithm in this validation study are: 9 out of 312 (2.9%) were TSI and Ferritin elevated with C282Y homozygosis. Seven of them proved to have HIO by MRI, PPV = 77.8% (45.3 to 93.7). 218 (69.9%) had TSI or Ferritin within normal values. Eleven of them had HIO NPV = 95% (91.2 to 97.2). 85 patients of our sample (27.2%), less than 1/3, needed to have a diagnostic MRI for HIO.

**Conclusion:** MRI is not necessary in 72.8% of the patients for HIO diagnosis. MRI is indicated in patients not C282Y homozygous with raised TSI and Ferritin.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0025 INCREASED FREQUENCY OF KERATIN 8/18 VARIANTS IN CHINESE NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS: AN ASSOCIATION WITH METABOLIC DISORDERS


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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) has the highest incidence of liver disease in Chinese population. Patients with NAFLD not only suffered from liver damage but a multisystem disorder with effects on the cardiovascular system, endocrine system, and kidneys. Keratins 8 and 18 (K8/K18) variants are considered to be involved in kinds of liver disorders and associated with the severity. Our study is the first to identify increased frequency of K8/K18 variants in NAFLD patients.

**Aims & Methods:** We analyzed the entire K8/K18 coding regions (15 exons and exonic-intronic boundaries) in 131 NAFLD patients and 173 controls. PCR-amplified samples were analyzed by DNA sequencing.

**Results:** We identified keratin heterozygous variants in 6 of 131 NAFLD patients (4%), including 2 amino-acid-altering heterozygous variants and 4 non-coding heterozygous variants. One novel amino-acid-altering heterozygous variant (K18 N193S) and three non-coding variants were observed. We found increased frequency of variants in NAFLD patients versus controls (4% vs. 0.58%, $P = 0.021$). Notably, keratin variants significantly associated with homeostatic model assessment-insulin resistance (HOMA-IR) in NAFLD patients (14.3% variants in NAFLD with IR versus 0.58% in control group, $P < 0.001$; 14.3% variants in NAFLD with IR versus 0.00% in NAFLD without IR, $P < 0.001$). Moreover, HOMA-IR and total cholesterol (TC) are higher in patients with keratin variants (HOMA-IR $2.93 \pm 1.26$ vs. $3.92 \pm 1.48$, $P = 0.029$; TC $5.76 \pm 1.03$ vs. $6.84 \pm 1.79$, $P = 0.015$).

**Conclusion:** There is an increased frequency of keratin 8/18 variants in NAFLD patients, and high levels of IR and TC of variant carriers are found suggesting an association with the severity of metabolic disorders.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0026 ASSESSMENT OF THE CLINICAL IMPACT OF MULTIDRUG-RESISTANT BACTERIA IN CIRRHOTIC PATIENTS


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**Introduction:** Bacterial infections are common in cirrhotic patients and are associated with poor prognosis. Literature reports an increasing incidence of infections by multidrug-resistant bacteria (MDR) in this group of patients, compared to the general population. The real clinical impact of these bacteria on short and medium term prognosis is not fully established. [1–2].

**Aims & Methods:** 1) to analyze at admission the incidence of MDR-bacteria in patients with decompensated cirrhosis; 2) to identify predictive factors for its development; 3) to study its impact in 30 and 90-day mortality. Retrospective cohort study, conducted in 2 centers that evaluated hospitalizations for decompensated cirrhosis between 2011 and 2014. We excluded patients without microbiological cultures at admission. MDR-bacteria were defined as strains resistant to at least three of the main antibiotic families including beta-lactam. Diagnosis of infections at admission (<24 h) was made according to conventional criteria.

**Results:** We identified a total of 779 hospitalizations, from those 349 patients met criteria for infection at admission (nosocomial: 27.5%). The 30 and 90-day mortality was 17.7% and 37.3% respectively. The most common infection was spontaneous bacterial peritonitis (n = 122), followed by urinary tract infections (n = 93) and pneumonia (n = 55). We obtained a total of 161 microbiological isolations (gram negative bacteria: 52.2%) from which 67 were considered to be MDR-bacteria; in 18.18% of the community-acquired infections was isolated a MDR-bacteria and 20.93% in the nosocomial-acquired group. There was no predominance of any gram class when evaluated MDR-bacteria ($p = 0.525$), and the most frequent isolated bacteria were extended spectrum beta lactamase positive *Escherichia coli* (n = 22), *Enterococcus faecalis* (n = 16) and methicillin resistant *Staphylococcus aureus* (n = 8). No statistical significantly difference was noticed between centers, when analyzed microbiological isolations rate. In multivariate analysis, we failed to identify risk factors for the development of MDR-bacteria (studied variables: hospitalization in the last 3 months; primary or secondary prophylaxis of spontaneous bacterial peritonitis; use of systemic antibiotics and gastrointestinal bleeding in the last month; continuous use of proton pump inhibitors in the last 3 months). In the univariate analysis, MDR-bacteria isolation were not associated with increased mortality at 30 ($p = 0.159$) neither at 90 days ($p = 0.673$), but they were associated with an increased length of hospitalization (MDR = 17.88 vs multidrug-susceptible strains = 13.80 days; $p = 0.045$).

**Conclusion:** 1) we identified a high and worrisome prevalence of MDR-bacteria in our sample (42.1% of the total bacterial microbiological isolations; community-acquired infections: 18.18%); 2) we failed to identify risk factors for its development, possibly because of the retrospective nature of our study, the heterogeneity of the infections that were evaluated and patients could had a previous colonization by MDR-bacteria without developing an active infection until an unbalancing event occurred; 3) microbiological isolation of a MDR-bacteria was not associated with a higher 30 or 90-day mortality. The results of this study which derive from a two-center retrospective experience, with a specific epidemiological pattern of multiresistance, cannot be fully generalized; however it indicates an alarming pattern of infections by MDR-bacteria on community-acquired infections, challenging the current international guidelines for bacterial infections in cirrhotic patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0027 EFFECTIVENESS OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNTS (TIPS) USING BARE METAL AND COVERED STENTS FOR THE TREATMENT OF VARICEAL BLEEDING IN CIRRHOSIS


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**Introduction:** Variceal hemorrhage is a frequent and severe complication in patients with cirrhosis and portal hypertension. Transjugular intrahepatic portosystemic shunts (TIPS) are used for treatment of severe acute variceal bleeding episodes or in patients with failure of secondary prophylaxis.
**Aims & Methods:** In this retrospective cohort study, cirrhotic patients undergoing TIPS implantation in two specialized centers in Vienna in 1994–2014 for secondary variceal bleeding prevention were included. Variceal re-bleeding events, TIPS patency, mortality and transplant free survival (TFS) were evaluated.
**Results:** 286 cirrhotic patients received TIPS for secondary prophylaxis of variceal bleeding. During a median (transplant-free) follow-up of 821 days, 67 patients (23%) experienced at least one re-bleeding event. Patients with isolated esophageal varices were at highest risk of re-bleeding (85% occurred in esophageal varices, 0% in isolated gastric varices, 15% in unspecified locations). Patients with expanded polytetrafluorethylene (ePTFE)-covered stents ($n = 167$) were at significantly lower risk for variceal re-bleeding than patients with bare-metal stents [$n = 119$; 14% vs. 37%, respectively, $p < 0.001$; OR at 1 year: 0.259 (95% confidence interval: 0.123–0.542, $p < 0.001$)]. Conversely, revisions due to shunt dysfunction were more common in bare metal than in ePTFE- stents (24% vs. 14%, respectively; log-rank: $p = 0.011$). More patients without re-bleeding within 1 year received non-selective beta blockers (NSBB) than re-bleeders (16% vs 6%, $p = 0.059$). Although overall transplant-free survival was similar between groups (47.4 vs. 43.6 months for ePTFE vs Bare stents; log-rank: $p = 0.968$), patients with ePTFE-covered stents were at lower risk of overall 1- and 2-year mortality compared to patients with bare stents (19% vs. 31%, $p = 0.020$ and 29% vs. 40%; $p = 0.041$, respectively).
**Conclusion:** TIPS prevent variceal re-bleeding in up to 77% of all patients. ePTFE stents are more effective at preventing variceal re-bleeding than bare-metal stents due higher patency rates. As a result, 1- and 2-year mortality rates were lower in ePTFE stents.
**Disclosure of Interest:** M. Schoder: Speaker honorarium (W. L. Gore & Associates).
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T. Reiberger: Speaker honorarium (W. L. Gore & Associates).
All other authors have declared no conflicts of interest.

### P0029 CYSTATIN C A REAL-TIME BIOMARKER FOR GLOMERULARFILTRATION RATE IN CRITICALLY-ILL PATIENTS WITH END STAGE LIVER DISEASE


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**Introduction:** Parameters allowing regular evaluation of renal function in critically ill patients such as serum creatinine and blood urea are not optimal. Sudden changes in glomerular filtration rate (GFR) are not followed by parallel changes in serum creatinine and are at risk of developing renal dysfunction.
**Aims & Methods:** The aim of study was to analyze the utility of serum cystatin C as a real-time biomarker of renal function in critically-ill patients with end stage liver disease (ESLD). **Patients and Methods:** serum creatinine, cystatin c and 24 hours creatinine clearance were determined daily to 300 patients (220 male and 80 female) critically ill patients with ESLD. The serum levels of creatinine and cystatin c were correlated with the creatinine clearance daily. The diagnostic value of serum creatinine and cystatin c to identify GFR under 80 ml/min per 1.73 $m^2$ was evaluated using receiver operating characteristic (ROC) curve analysis.
**Results:** Thirty out of 300 patients (10%) had serum creatinine above the upper limit of normal, while 85 out of 300 patients (28.3%) had serum cystatin c above the upper limit of normal. Statistically the ability of serum cystatin c to identify a creatinine clearance rate 80 ml/min per 1.73 $m^2$ was better than that of serum creatinine (areas under the ROC curve: for cystatin c 0.925, and for creatinine 0.613).
**Conclusion:** Serum cystatin c is an accurate easy and useful marker, better than serum creatinine to detect early renal dysfunction in real-time before acute renal injury in critically-ill patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0031 NEW TREATMENT WITH SULODEXIDUM FOR PORTAL VEIN THROMBOSIS IN PATIENTS WITH LIVER CIRRHOSIS


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**Introduction:** Vitamin K antagonists and low-molecular weight heparin are not ideal drugs for patients with cirrhosis and portal vein thrombosis. New drugs must be investigated, based on the concept of rebalanced hemostasis in patients with liver disease.
**Aims & Methods:** We intended to assess the safety and efficacy of sulodexidum to treat portal vein thrombosis (PVT) in cirrhotic patients. From June 2010 to March 2013, 810 patients with liver cirrhosis admitted to our clinic received Doppler ultrasound examination as a part of routine workup. In the presence of PVT, spiral CT or magnetic resonance was performed to exclude concomitant hepatocellular carcinoma and to evaluate the extension of thrombosis in the portal-splenic-mesenteric axis. 94 patients diagnosed with non-neoplastic PVT and cirrhosis were prospectively enrolled (50 in the treatment group with sulodexidum 2 tb/day and 44 in the control group). In 55.3% of patients, PVT was an occasional finding, 12.8% presented with acute abdominal pain, while in 32.1% with bleeding from gastro-esophageal varices. In this last group, treatment was started after endoscopic eradication of varices by band ligation. In the treatment group, 16 patients (32%) had complete PVT and 34 pts (68%) had partial PVT. The mean MELD score was 14.6. Therapy was administered for a median period of 12 months and individuals were followed for a median time of 19 months.
**Results:** Complete recanalization of the portal vein occurred in 24% vs 0% of subjects, partial recanalization in 38% vs 27.2% of pts, and no response in 38% vs 72.8%. No significant side effects, particularly bleeding complications, were observed during therapy. The median value of platelets was 58, 000/$mm^3$ and 55, 000/$mm^3$ at the end of treatment. 4 of 28 pts who stopped treatment showed re-thrombosis of the portal vein at 1, 4 and 6 months. In univariate analysis, previous bleeding caused by portal hypertension and time between diagnosis and initiation of treatment $< 14$ days were positively associated with PV recanalization. Decompensation occurred during the study period significantly more in placebo than in sulodexidum treated patients [placebo 18/44 (40.9%) vs 11/50 (22%); $p = 0.01$].
**Conclusion:** Sulodexidum demonstrated to be safe and effective in the treatment of PVT in patients with liver cirrhosis, and delayed liver decompensation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0032 IS IT TIME TO CONSIDER ANTITHROMBOTIC PROPHYLAXIS IN CHRONIC LIVER DISEASE?: USEFULNESS OF CHA2DS2-VASC SCORE, HAS-BLED SCORE AND PLATELET COUNT

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**Introduction:** Liver plays a central role in maintaining hemostasis. The imbalance between coagulation-anticoagulation can occur in Chronic Liver Disease (CLD). Antithrombotic prophylaxis in CLD remains to be established.
**Aims:** To evaluate the prevalence and predictive scores of vascular events in CLD and prognostic implication.
**Methods:** Case-control retrospective study of 200 patients with CLD, divided in 3 groups: with thrombotic events, bleeding events and with no thrombotic or bleeding events. The variables included, prior to vascular events, were age, gender, coagulation parameters, CLD prognostic scores (Child-Turcotte-Pugh (CPT), MELD, Na-MELD, APRI, AST/ALT ratio, ALT/AST ratio, Age to platelet index, Bonacini cirrhosis discriminant score, Pohl score, king score, FIB-4, FI score), predictive scores of bleeding (HAS-BLED) and thrombotic (CHA2DS2-VASc), and overall or vascular events-related mortality.
**Results:** About half (99/200) of patients developed vascular events, thrombotic in 32.3% (32/99) and hemorrhagic in 77.8% (77/99), with both of them in 10 patients. After multivariate analysis, the independent predictors of bleeding events in CLD were high HAS-BLED score ($3.9 \pm 1.0$vs$3.0 \pm 1.1$; OR 2.105; $p < 0.001$) and low platelet count ($93.3 \pm 45.9$vs$118.2 \pm 67.1$; OR 1.008; $p = 0.006$); and of thrombotic events were high CHA2DS2-VASc score ($3.0 \pm 2.0$vs$1.4 \pm 1.4$; OR 1.1773; $p < 0.001$) and high platelet count ($141.6 \pm 78.6$vs$102.3 \pm 55.0$; OR 1.009; $p = 0.002$). The best cut-off of HAS-BLED score was 3 (AUROC 0.707; $p < 0.001$; S63.6%; Sp65.6%), CHA2DS2-VASc 2 score was 2 (AUROC 0.731; $p < 0.001$; S75.0%; Sp60.5%) and platelet count was 103 (AUROC 0.648; $p = 0.008$; S62.5%; Sp61.3%). The remaining prognostic scores and other parameters of coagulation or liver function has not been associated with the development of vascular events. Only thrombotic events were associated with increased overall mortality and vascular events-related mortality (37.5% vs 21.4%; $p = 0.046$ and 18.8% vs 4.8%; $p = 0.012$).
**Conclusion:** Vascular events are common in CLD and include not only bleeding events, but also thrombotic events. Patients with CHA2DS2-VASc score $\geq 2$, HAS-BLED score $< 3$ and platelet count $> 103$ could benefit of prophylactic antithrombotic therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0033 CONTINUOUS PROTON PUMP INHIBITOR THERAPY INCREASES THE RISK OF BACTERIAL INFECTION IN CIRRHOTIC PATIENTS

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**Introduction:** Patients with cirrhosis have a high risk for developing bacterial infections. Worse liver function, history of recent hospitalization, previous spontaneous bacterial peritonitis and gastrointestinal bleeding are well documented risk factors for its development. Although proton pump inhibitors (PPI) are associated with dysbiosis and with increased intestinal permeability and transitory bacteriemia, it still remains unknown whether continuous PPIs exposure increases the risk for bacterial infections and literature reports conflicting results.[1–3].
**Aims & Methods:** 1) to evaluate if continuous exposure to PPIs is a risk factor for bacterial infections in cirrhotic patients with ascites; 2) to assess the effect of PPIs exposure in 30 and 90-day mortality. Retrospective cohort study that evaluated hospitalizations secondary to cirrhosis decompensation between 2010 and 2014 in a tertiary center. Only patients with ascites and microbiological cultures at admission were considered. Past medical history was reviewed: PPI exposure was defined as continuous exposure for at least 3 months; previous hepatic function was assessed by past medical history review and it was expressed according to Child-Pugh score. A multivariate analysis was conducted by binary logistic regression aiming risk factors for the presence of bacterial infections at admission.
**Results:** 571 admissions were evaluated, gastrointestinal bleeding was present in 137 episodes and 252 met criteria for infection at admission. The most common infection was spontaneous bacterial peritonitis (SBP, $n = 100$), followed by urinary tract infection ($n = 62$) and pneumonia ($n = 33$). When analyzed medical history: 51% were previously classified as Child-Pugh C patients; 127 had recent hospitalization ($< 3$ month), 51a previous SBP (47 doing secondary prophylaxis) and 9 a recent gastrointestinal bleeding episode ($< 1$ month); at admission an active neoplasia was present in 71 episodes (hepatocarcinoma $n = 65$); 180 met criteria for continuous exposure to PPI and 29 were taking beta-blockers. In multivariate analysis Child-Pugh C ($p = 0.000$; OR = 2.971), recent hospitalization ($p = 0.000$; OR = 3.188) and continuous exposure to PPIs ($p = 0.002$; OR = 1.924) were independent risk factors for bacterial infections. When analyzed the effect of previous PPIs exposure: 30-day mortality after admission was not statistically significant different ($p = 0.095$) between groups, but PPIs exposure was associated with a higher 90-day mortality ($p = 0.000$; OR = 1.893).
**Conclusion:** In our sample continuous exposure to PPIs was an independent risk factor for bacterial infections in cirrhotic patients with ascites and it was associated with a higher 90-day mortality. Therefore, the prescription of PPIs in cirrhotic patients with ascites should be considered carefully.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0034 IMPACT OF THE USE OF BETA-BLOCKERS IN DECOMPENSATED CIRRHOSIS

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**Introduction:** The benefit of the use of beta-blockers (BB) in the primary and secondary prevention of variceal bleeding in cirrhosis is a known fact. Additionally, a reduction on the risk of ascites, hepatorenal syndrome and spontaneous bacterial peritonitis (SBP) was also associated with BB in some studies. On the other hand, there are studies that indicate a detrimental effect of the use of BB in patients with decompensated cirrhosis, namely refractory ascites or SBP. As such, the existence of a "window of opportunity" in the natural history of cirrhosis for the use of BB was hypothesized.
**Aims & Methods:** The aim of this study was to evaluate the impact of the use of BB in patients hospitalized for decompensated cirrhosis. We performed a retrospective study with inclusion of all patients admitted in a gastroenterology and hepatology unit due to decompensated cirrhosis (ascites, variceal bleeding, encephalopathy, renal failure, jaundice and bacterial infections) between 01-01-2013 and 31-12-2015. Patients were evaluated in two different groups according to use of BB at admission. Demographic, clinical and therapeutic data, prognostic scores and hospitalization outcome were collected. Patients with incomplete medical records were excluded from the analysis. Statistical analysis was performed with SPSS 20.0.
**Results:** We identified 164 admissions fulfilling inclusion criteria, 34 of which (20.7%) corresponding to patients medicated with BB. Both groups (with and without BB) were homogeneous regarding demographic features, cirrhosis aetiology and Child-Turcotte-Pugh and MELD scores at admission. There were no differences in the duration of hospitalisation [median (interquartile range – IQR); with BB: 8 days (5–14); without BB: 8 days (6–11); $p = 0.74$)] or in the in-hospital mortality (with BB 14.7%; without BB 11.5%; $p = 0.57$) between the 2 groups. In the sub-analysis by reason for admission, there was a tendency to greater mortality in patients admitted for ascites medicated with BB [5.8% vs 1.5%; $p = 0.052$; OR 21; confidence interval 95% 1.27–346).
**Conclusion:** The use of BB in patients with decompensated cirrhosis admitted for ascites may lead to an increase in in-hospital mortality.
**Disclosure of Interest:** P. Ministro: Medical advisor for Abbvie, Ferring, MSD and Hospira.
All other authors have declared no conflicts of interest.

## P0035 EFFICACY OF TOLVAPTAN WITH CELL-FREE AND CONCENRATED REINFUSION THERAPY FOR REFRACORY ASCITES IN PATIENTS WITH ADVANCED LIVER DISEASE

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**Introduction:** In Japan, adding of tolvaptan (TLV), an oral vasopressin V2 receptor antagonist to conventional diuretics has been used for refractory ascites in patients with cirrhosis, however the effectiveness of TLV is limited in end-stage liver disease. Serial paracentesis provide relief of symptoms but also promote loss of albumin and hypovolemia, which may cause renal dysfunction. Cell-free and concentrated ascites reinfusion therapy (CART) is a treatment which maintains

albumin by filtration, concentration, reinfusion of drained ascites and avoids complications due to paracentesis. CART is listed in the clinical practice guideline for liver cirrhosis in Japan, however the efficacy of TLV with CART for the treatment of refractory hepatic ascites has not been elucidated.
**Aims & Methods:** The aims of this study were to identify predictors associated with the response to TLV in patients with decompensated cirrhosis and to evaluate the efficacy of TLV with CART in non-responders. TLV was administered to 28 liver cirrhosis patients with persistent ascites despite conventional diuretics. Responders who were defined as ≥1 kg body-weight reduction in 1 week continued to receive TLV. Non-responders underwent CART in addition to the treatment with TLV. Conventional diuretics continued throughout. We assessed predictors that contributed to the response to TLV using univariate analysis and multivariate logistic regression analysis. Changes in the clinically relevant parameters were evaluated prior to the use of TLV and 1 month later.
**Results:** Responders to TLV were 19 (67.9%) patients. Gender (male: 47 vs 89%, respectively in responders and non-responders, $p = 0.026$), etiology of cirrhosis (HCV: 42 vs 0%, $p = 0.021$, alcohol: 26 vs 78%, $p = 0.010$), baseline BUN (19.3 vs 44.2 mg/dl, $p = 0.024$) and baseline creatinine (0.88 vs 1.94 mg/dl, $p = 0.009$) were associated with response to TLV. By multivariate analysis, we determined that higher level of BUN ($p = 0.046$) was the independent predictor of non-response to TLV along with male gender ($p = 0.008$). In non-responders, the mean volume of collected ascites was 6543 ml per session, and non-responders underwent CART at the mean 1.3 sessions for 1 month in each patient. In patients treated using TLV with CART, estimate glomerular filtration rate (eGFR) significantly increased from 47.5 to 54.3 ml/min/1.73 $m^2$ 1 month after administration of TLV ($p = 0.020$) and the serum level of albumin was almost identical to that prior to administration of TLV (2.87 at baseline vs 2.94 mg/dl 1 month after administration of TLV, $p = 0.137$). TVL with CART alleviated symptoms such as abdominal fullness in all the patients. There were no serious adverse events during the entire treatment period.
**Conclusion:** Higher level of BUN is the predictor of non-response to TLV in patients with advanced liver disease. In non-responders to TLV, CART with TLV keeps serum level of albumin and avoids renal dysfunction; therefore, TLV with CART is useful for refractory ascites in patients with decompensated cirrhosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0036 MEAN PLATELET VOLUME IS A PROMSIDING DIAGNOSTIC MARKER FOR SYSTEMIC INFLAMMATION IN CIRRHOTIC PATIENTS WITH ASCITIC FLUID INFECTION


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**Introduction:** Spontaneous bacterial peritonitis (SBP) is the most frequent and life-threatening infection in patients with decompensated liver cirrhosis. Diagnosis should be prompt and treatment must not be delayed until the microbiology results are available. Mean platelet volume (MPV) is one of the most widely used surrogate markers of platelet activation. MPV might be helpful in early diagnosis of SBP which may result in improved patient outcome.
**Aims & Methods:** The current study was conducted to assess the potential role that MPV may have in the diagnosis of SBP in cirrhotic patients with ascites together with other inflammatory markers; ESR &CRP. The current study is a case control study that was conducted from May 2015 to March 2016 at the Endemic Medicine and Hepatology departments, in both Ain Shams and Cairo Universities. Three groups were included in the study. Group I (SBP group) included 100 patients with liver cirrhosis and ascites complicated by SBP, group II (non-SBP group) included 98 patients with liver cirrhosis and ascites without SBP and group III included 50 healthy subjects to serve as a control group. Patients were subjected to thorough history taking, clinical examination and laboratory evaluation. ESR, CRP and Complete blood picture including MPV was done at time of diagnosis of SBP.
**Results:** Platelet count was significantly lower in SBP group than in non-SBP group (median 116.5 vs. 150 with P value $< 0.01$). On the other hand, ESR, CRP and total leucocytic count (TLC) in ascitic fluid were significantly higher in SBP group compared to non-SBP group (median 37.5 vs. 12, 12 vs. 5 and 530 vs. 60 respectively with p value $< 0.01$). On the other hand, hemoglobin, bilirubin, albumin, INR, creatinine and Child-Turcotte-Pugh (CTP) Score showed no statistically significant difference between SBP and non-SBP groups. The MPV was significantly higher in SBP group vs. non-SBP group and healthy control group (8.5, 7.9 and 8.3 respectively and P value $< 0.0001$). On constructing ROC curve for the MPV; at a cutoff value of 8.4 fl, MPV had 73% sensitivity and 85.7% specificity for detecting SBP with overall accuracy 79.3%, [AUC = 0.84 with negative predictive value (NPV) and positive predictive value (PPV) for MPV of 75.7 and 83.9%, respectively]. Regarding ESR; at a cutoff value of 20, ESR had 78% sensitivity and 63.4% specificity for detecting SBP with overall accuracy of 70.7%, [AUC = 0.845 with negative predictive value (NPV) and positive predictive value (PPV) for MPV of 73.8 and 68.5%, respectively]. Regarding CRP; at a cutoff value of 7, MPV had 66% sensitivity and 67.4% specificity for detecting SBP with overall accuracy 66.6%, [AUC = 0.71 with negative predictive value (NPV) and positive predictive value (PPV) for MPV of 66% and 67.3%, respectively].
**Conclusion:** MPV is increased in SBP in cirrhotic patients with ascites than the other inflammatory markers; ESR & CRP. It can be used as an accurate predictor test of ascitic fluid infection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0037 EVALUATION OF AN ALTERNATIVE MODEL TO MELD FOR ANTICOAGULATED PATIENTS WITH CIRRHOSIS: MELD-XI (EXCLUDING INR)


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**Introduction:** The concept of the existence of a "natural anticoagulation" state in patients with cirrhosis is outdated, and it's now widely accepted that there is a dynamic and precarious hemostatic balance in this group of patients. Therefore, anticoagulant agents such as warfarin are being increasingly used in cirrhotic patients. However, one of the most used prognostic models, the Model for End-stage Liver Disease (MELD) is based on the values of bilirubin, creatinine and INR, and no modification exists for anticoagulated patients. As such, there might be an overestimation of risk in these group of patients when using MELD, so that a new model not including INR is necessary. MELD-XI (eXcluding INR) is a model based exclusively on bilirubin and creatinine, and may be a potential alternative.
**Aims & Methods:** The aim of this study was to compare MELD and MELD-XI scores on the evaluation of risk of mortality in patients admitted for decompensated cirrhosis. We performed a retrospective study with inclusion of patients admitted in a gastroenterology and hepatology unit for decompensated cirrhosis (including but not limited to patients with acute-on chronic liver failure) between 2013 and 2015. Patients with hepatocellular carcinoma, portal vein thrombosis and those submitted to liver transplantation within 3 months of admission were excluded from the analysis. MELD score was calculated according to the formula and criteria defined by United Network for Organ Sharing. MELD-XI was calculated according to the formula 5.11xLn (bilirubin) + 11.76xLn (creatinine) + 9.44 previously described. Mortality within 3 months of admission (M3) was evaluated. Statistical analysis was performed with SPSS 20.0.
**Results:** One hundred and twenty three hospital admissions corresponding to 87 patients were identified. MELD-XI had a weak discrimination power for M3 with an area under the receiver operating characteristics curve (AUROC) of 0.68 [confidence interval (CI) 95% 0.57–0.79; $p = 0.006$) versus 0.73 (CI 95% 0.63–0.84; $p = 0.001$) for MELD. On the sub-analysis by type of decompensation, MELD-XI had the best discrimination power for M3 in the sub-group of patients with ascites with an AUROC of 0.87 (CI95% 0.0–1.0; $p = 0.028$). We performed a Spearman correlation to ascertain the relationship between the two models, in order to understand if the exclusion of INR had a significant impact on the prognostic model. There was a positive, statistically significant and strong correlation between MELD and MELD-XI ($r = 0.90$; $p < 0.001$).
**Conclusion:** In this population both MELD and MELD-XI had a weak discrimination power for the prediction of mortality at 3 months. However the correlation between the two models was strong, so in anticoagulated patients MELD-XI can be a valid alternative to MELD.
**Disclosure of Interest:** P. Ministro: Medical advisor for Abbvie, Ferring, MSD and Hospira.
All other authors have declared no conflicts of interest.

## P0038 INCIDENCE AND PREDICTORS OF REBLEEDING AFTER BAND LIGATION IN PATIENTS WITH ACUTE ESOPHAGEAL VARICEAL BLEEDING

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**Introduction:** Variceal bleeding (VB) occurs in 25 to 40% of patients with portal hypertension. Endoscopic variceal ligation (EVL) is the method of choice for the treatment of esophageal varices but there are no specific guidelines about the number of bands per treatment. Some authors reported that the fewer bands placed the more rebleeding risk. Rebleeding occurs in the first few weeks after EVL, with a range of mortality of 30–50%.
**Aims & Methods:** The primary aim for this study was to assess incidence and risk factors contributing to variceal rebleeding (VRB) after EVL, and the role of the number of rubber bands in relapse. We also analyzed the correlation between the VRB and the use of proton pump inhibitors (PPIs), beta-blockers (BB), the Child Turcotte Pugh classification (CTP) and MELD score. This was a retrospective study in patients with liver cirrhosis and VB admitted to our Unit between January 2012 and December 2015.
**Results:** We included 75 patients, of whom 88% ($n = 66$) were male, with an average age of $60.51 \pm 11.39$ years old. 61% of patients had alcoholic cirrhosis and 12% viral etiology. An average of 6.48 (3–12) bands was placed in the first session of EVL. Active bleeding was observed in 38.6% patients. After the procedure 90% were treated with PPIs and 68% with BB. The most common comorbidities were diabetes mellitus ($n = 31$) and essential hypertension ($n = 24$). We observed VRB in 24% of patients ($n = 18$), and was higher in patients with CTP class B and C ($n = 15$, $p = 0.015$) and in patients with less than 6 bands placed ($n = 13$, $p = 0.018$). There was no statistical difference between the VRB with use of PPIs, BB, MELD score or hepatocellular carcinoma at time of diagnosis.
**Conclusion:** This study results contradict the literature regarding the influence of a higher number of bands as a bleeding predictor factor in VRB. In our group we concluded that the CTP B our C class was a VRB predictor.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0039 MORTALITY AFTER THE FIRST ADMISSION FOR HEPATIC ENCEPHALOPATHY

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**Introduction:** Port-systemic hepatic encephalopathy (PSHE) is one of the most common complications in liver cirrhosis. The development of hepatic encephalopathy negatively impacts patient survival. The occurrence of encephalopathy severe enough to lead to hospitalization is associated with a survival probability of 42% at 1 year of follow-up.
**Aims & Methods:** AIMS: Assess the factors associated with increased one year mortality after hospital admission for PSHE. METHODS: Retrospective analysis of admissions for EHPS of patients with liver cirrhosis, between October 2011 and October 2014. Only the onset episode was included. Patients were followed during 1 year. Descriptive statistics, uni and multivariate analysis, logistic regression and ROC curves analysis were performed using IBM SPSS Statistics 22 with $p < 0.05$ deemed to be statistically significant.
**Results:** During the period of the study there were 120 patients discharged with onset PSHE, 78% were men with a mean age of $59 \pm 14$ years, 97% had Child-Pugh B/C, 55% had alcoholic liver disease and 10% had hepatocellular carcinoma. The overall mortality rate during the first year of follow-up was 46%. These patients were 80% men with mean age of $59 \pm 17$ years. Mortality was higher in patients with higher MELD, MELD-Na and Child-Pugh scores ($p < 0.001$), hepatocellular carcinoma ($p = 0.033$), ascites ($p = 0.008$) and readmission for PSHE ($p = 0.025$). Patients with hyponatremia ($p = 0.006$) and higher initial degree of PSHE ($p = 0.036$) in onset episode also had a higher mortality rate. Patients who underwent antibiotic therapy in the first admission for PSHE ($p < 0.001$) had a lower mortality. In the multivariate analysis, there was an independent association between mortality in the follow-up and higher MELD score ($OR = 1.2$; $p = 0.001$), Child-Pugh C ($OR = 3.5$, $p = 0.008$) and readmission for PSHE ($OR = 3.1$, $p = 0.02$).
**Conclusion:** Our data reveals to be similar to that found in the literature, showing that PSHE requiring hospitalization was associated with a poor prognosis, with a one year mortality rate of 46%. The readmission for PSHE and higher Child-Pugh and MELD scores were independently associated with a higher mortality rate.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0040 SEXUAL DYSFUNCTION IN CHRONIC LIVER DISEASE: IS IT A HOT TOPIC FOR CIRRHOTIC PATIENTS?

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**Introduction:** Sexual activity is a crucial component of human relationships and has an important impact on quality of life [1]. Despite of its importance, it is rarely evaluated in clinical practice, especially in patients with chronic liver disease (CLD).
**Aims & Methods:** The aim of this study was to evaluate the importance of this issue in a population with chronic liver disease (CLD). This is a cross-sectional study based on an opinion questionnaire, in male consecutive patients, followed as outpatients in a Hepatology Department. The sexual dysfunction was also assessed through the simplified version of the International Index of Erectile Function questionnaire. Statistics analysis were performed using IBM SPSS Statistics 22 with $p < 0.05$ deemed to be statistically significant.
**Results:** A total of 67 male patients were surveyed, 57% with liver cirrhosis, median age of 56 years (IQR: 48–62) and median number of years of education was 7 years (IQR: 5–12). Forty-one patients (62.1%) fulfilled criteria for erectile dysfunction (ED). Sixty-four percent of patients considered that the sexual dysfunction issue should be asked during the Hepatology consultation. The majority of patients (73%), described themselves as being ''very comfortable'' to address this issue, with no statistically significant differences between patients with or without ED (ED: 87.5% vs. Non-ED: 91.3%, $p = 1.000$). Evaluating all the patients surveyed, 45.3% did not consider that the CLD could interfere with ED. However, in 62.1% of the patients whose assessment was consistent with ED, 62.1% considered that CLD could interfere with their sexual dysfunction ($p < 0.001$). When asked about the association between the use of drugs, only 32.5% reported that the medication they took could negatively correlate with his sexual function, and 50% of those who used beta-blockers reported a positive association between therapy and the presence of ED ($p = 0.148$). The answers did not differ statistically significantly with the level of education and marital status.
**Conclusion:** The majority of patients with ED positively correlated this condition with liver disease. The high prevalence of ED in this cohort highlights the importance of addressing this issue at the Hepatology consultation in order to provide a specific treatment for this condition.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0041 REAL-LIFE PRACTICE OF CHRONIC HEPATITIS C PATIENTS TREATED WITH DIRECT ACTING ANTIVIRALS (DAAS) IN A TERTIARY CENTER OF PORTUGAL

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**Introduction:** The use of new DAAs deeply changed the treatment of chronic hepatitis C virus (HCV) infection in terms of efficacy and tolerability. However, there is still lack of information regarding the real-life data.
**Aims & Methods:** Our aims are to investigate clinical and laboratorial impact, effectiveness and adverse effects of these drugs in real-life practice, in a tertiary center of Portugal. This observational prospective study included all patients who underwent treatment with DAAs (including sofosbuvir) in our department since February 2015. The patients variables were collected in terms of demography and HCV infection baseline characteristics (genotype, viral load, elastography, laboratorial tests and previous treatments). Regarding the treatment, data about therapeutic regimens, sequencial laboratorial follow-up and adverse effects were collected. The variables were compared before and after treatment for

patients who achieved 12 weeks post-treatment evaluation, corresponding to the sustained virological response (SVR) time. The statistic analysis used the logistic-binary regression test and Kaplan-Mayer curves, depending on the specific analyzed variables.
**Results:** A total of 642 were included in our study in which SVR was achieved in 96.7%. The average of age was 53.8 years-old and 64.5% were men. The genotypes related to HCV infection were: 1 in 70.2%, 2 or 3 in 12.8% and 4 in 16.8%. Cirrhotic patients (elastrography > 12.5 Kpa) represented 34.1% of the sample. The majority of patients were treated with sofosbuvir-ledipasvir combination (n = 580; 90.3%) and in 21.9% of patients ribavirin was used in concomitancy. The genotypes 1 and 4 revealed better outcomes in terms of SVR analysis, 97.1 and 95.7, respectively. The genotype 3 achieved 90.2% of SVR. During the treatment the hemoglobin and platelet count decreased independently on ribavirin use ($p < 0.001$). And the liver tests before and after treatment showed a decreased in ALT ($p < 0.001$), GGT ($p < 0.001$) and ALP ($p = 0.004$) levels. Preliminary study of elastrography values revealed a decreased of fibrosis in cirrhotic patients ($p = 0.002$; N = 44). There was no relation between viral load at 2 and 4 weeks of treatment and the final response status. Adverse effects with therapy withdrawal were rare and occurred in 5 patients (0.8%).
**Conclusion:** Treatment with DAAs was highly effective and safe in our patients. Almost all liver tests were improved after this therapy. Evaluation of viral load at 2 and 4 weeks of therapy did not predict the final response.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0042 GENDER-DEPENDENT DRUG–DRUG INTERACTIONS (DDIS) WITH NOVEL ALL ORAL HCV THERAPIES IN GERMAN REAL WORLD: LOW FREQUENCY OF DDIS WITH ELBASVIR (EBV) AND GRAZOPREVIR (GRZ)

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**Introduction:** A high frequency of clinically relevant DDIs between the regular outpatient medications and direct-acting antivirals (DAAs) has been reported for HCV treatment with sofosbuvir (SOF) in combination with simeprevir (SMV), daclatasvir (DCV) or ledipasvir (LDV) (30–40%) while patients (pts) treated with ombitasvir/paritaprevir/ritonavir (OBV/PTV/r) ± dasabuvir (DSV) had a risk > 60% (Clin Infect Dis 2016; 62: 561–567). However, the number of DDIs might have been overestimated in this single center study at a tertiary referral center because of a high frequency of severe cases. We therefore assessed the clinical relevance of DDIs between the regular outpatient medications and the above HCV therapies together with the recently approved therapy with EBV/GRZ in a large multicenter real-world cohort.
**Aims & Methods:** From April 2012 until January 2014, regular outpatient medications were documented from 505 pts with HCV G1 infection by 91 medical practices and hospital outpatient departments in Germany. Clinically relevant DDIs (co-administration of drugs contraindicated or may require dose adjustment/closer monitoring) were assessed based on information available at www.hep-druginteractions.org and the prescribing information for each drug in April 2016.
**Results:** The mean age of 505 enrolled pts was 47 years, 60% male, 12% were under opioid substitution, 4% had HIV co-infection, 8% had cirrhosis and 34% had failed prior antiviral therapy. 43% of pts did not take any drugs regularly while 48% reported the regular intake of 1–3 drugs and 9% of 4 or more drugs. The following frequencies of relevant DDIs between the regular outpatient medications and the different antiviral regimens were found: SOF/SMV 28%, SOF/DCV 28%, SOF/LDV 31%, OBV/PTV/r 42% and OBV/PTV/r + DSV 41%. In contrast, a low DDI frequency of only 5% was found for EBV/GRZ. Interestingly, higher frequencies of DDIs were observed in female pts when compared with male pts: SOF/SMV 35 vs. 24%, SOF/DCV 39 vs. 21%, SOF/LDV 35 vs. 29%, OBV/PTV/r 55 vs. 33%, OBV/PTV/r + DSV 54 vs. 33% and EBV/GRZ 7 vs. 3%.
**Conclusion:** Clinically relevant DDIs between the regular outpatient medications and SOF or OBV treatment regimens are a common problem in pts undergoing HCV G1 treatment in German real life. DDIs seem to occur more frequently in female pts suggesting a role for gender-related outpatient medications. Compared to SOF or OBV treatment regimens, there is a 6–8 fold lower frequency of clinically relevant DDIs between outpatient medications and the novel HCV therapy with EBV/GRZ.
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## P0043 HIGH POTENTIAL FOR DRUG-DRUG INTERACTIONS (DDIS) DURING CHRONIC HEPATITIS C (CHC) THERAPY WITH DIRECT ACTING ANTIVIRALS (DDAS) IN ROUTINE CLINICAL PRACTICE

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**Introduction:** Several clinical trials and real-life cohorts have shown that therapy with DAAs is safe, well tolerated and effective in the majority of CHC patients. The main limitation of DAAs is their potential for DDIs, the probability of which has not been properly assessed in routine clinical practice.
**Aims & Methods:** We aimed to determine the risk of possible DDIs with all HCV agents in 500 consecutive CHC patients (mean age 49 ± 14 years, M/F: 322/178) seen in 2015 at the outpatient liver clinics of 5 tertiary liver centers in Greece (100 patients from each center). Patients with HIV coinfection were excluded. Patients' demographics and habits, laboratory parameters, HCV and liver disease characteristics as well as concomitant diseases and chronic use of drugs were collected from patients' records. All concomitant drugs chronically used by the patients were classified into those with no/no clear data for DDIs, potential DDIs and contraindication for each of the HCV agents according to the HEP Drug Interaction Checker (University of Liverpool).
**Results:** In total, 326 (65%) patients reported no chronic drug use. Patients with contraindications to HCV agents due to DDIs were 30 (6.0%) for paritaprevir/ritonavir/ombitasvir ± dasabuvir (3D/2D), 26 (5.2%) for boceprevir/telaprevir (BOC/TPV), 10 (2.0%) for simeprevir (SMV), 2 (0.4%) for sofosbuvir (SOF) or daclatasvir (DCV) or ledipasvir/sofosbuvir (LDV/SOF) and none for peginterferon (pegIFN) or ribavirin (RBV) ($P < 0.001$). Contraindications due to DDIs or potential DDIs were present more frequently for NS3 protease inhibitors containing agents (22.8–27.0%) than NS5A inhibitors ± SOF (16.8–17.4%, $P \leq 0.040$ vs NS3 inhibitors) than SOF (11.8%, $P < 0.001$ vs NS3 inhibitors; $P \leq 0.030$ vs NS5A inhibitors) or RBV (11.2%, $P \leq 0.014$ vs NS3/NS5A inhibitors) than pegIFN (7.6%, $P < 0.001$ vs NS3/NS5A inhibitors; $P = 0.033$ vs SOF; $P = 0.065$ vs RBV) (Table). Contraindications/Potential DDIs were present more frequently in patients ≥ 50 than < 50 years old for all HCV agents ($P \leq 0.034$), with F3-F4 than F0-F2 fibrosis for all agents ($P \leq 0.014$) except pegIFN and RBV, with F4 than F0-F3 fibrosis for all agents ($P \leq 0.019$) or with genotype (G) 1/4 than 2/3 for all agents ($P \leq 0.036$) except pegIFN, LDV/SOF and 3D/2D (Table)..
**Conclusion:** In the current DAAs era, the potential for DDIs represents one of the main challenges in the management of CHC patients in routine clinical practice, being present more frequently compared to the pegIFN + RBV era. Contraindications/Potential DDIs are present more frequently (~25%) for NS3 inhibitors, but also for NS5A inhibitors (17%) and SOF (12%); their probability is higher for patients with priority for DAAs therapy (eg advanced liver disease) and therefore caution is always warranted.
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C. Tsoulas: Gilead: employee.

**Abstract No: P0043**
**Table:** Patients with contraindications due to DDIs or potential DDIs to HCV agents.

| | Pts, n | PegIFN | RBV | BOC/TPV | SMV | SOF | DCV | LDV/SOF | 3D/2D |
|---|---|---|---|---|---|---|---|---|---|
| All pts | 500 | 7.6% | 11.2% | 27.0% | 22.8% | 11.8% | 17.4% | 16.8% | 27.0% |
| Age ≥ 50 < 50 | 253 247 | 11.5% 3.6% | 15.4% 6.9% | 32.0% 21.9% | 27.7% 17.8% | 15.0% 8.5% | 22.5% 12.1% | 22.1% 11.3% | 34.0% 19.8% |
| F0-2* F3-F4* | 226 224 | 6.2% 10.3% | 9.3% 14.3% | 22.6% 34.4% | 17.7% 30.4% | 8.4% 16.5% | 12.8% 23.7% | 13.3% 22.8% | 23.0% 35.3% |
| F0-3* F4* | 306 144 | 5.9% 13.2% | 8.5% 18.8% | 24.5% 36.8% | 20.6% 31.3% | 9.2% 19.4% | 14.1% 27.1% | 14.1% 26.4% | 23.9% 40.3% |
| G1/4# G2/3# | 286 210 | 9.8% 4.8% | 14.7% 6.7% | 31.1% 21.4% | 26.9% 17.1% | 14.7% 8.1% | 22.4% 11.0% | 18.9% 14.3% | 29.4% 23.8% |

*Fibrosis stage was unknown in 50 patients (pts); #Genotype was unknown in 4 pts. In multivariate analyses, presence of contraindications/potential DDIs was independently associated with G1/4 for RBV or SMV, F3-F4 or F4 fibrosis for BOC/TPV or SOF, G1/4 and F3-F4 or F4 fibrosis for DCV and F4 fibrosis for LDV/SOF or 3D/2D.

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## P0044 SOFOSBUVIR PLUS RIBAVIRIN FOR TREATMENT OF CIRRHOTIC HCV PATIENTS GENOTYPE-4

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**Introduction:** Egypt has the highest hepatitis C virus prevalence in the world. Sofosbuvir is a new highly effective drug for treatment of hepatitis C virus (HCV) infection. Compared to previous treatments, sofosbuvir-based regimens provide a higher cure rate, fewer side effects, and a two- to four-fold reduced duration of therapy.
**Aims & Methods:** The aim of the study was to evaluate the antiviral efficacy, safety, and tolerability of sofosbuvir (SOF) plus ribavirin (RBV) in Egyptian patients with liver cirrhosis due to chronic hepatitis C virus (HCV) infection. We studied 2400 cirrhotic Egyptian patients with chronic HCV infection treated with dual therapy with Sofosbuvir and ribavirin for 24 weeks. Efficacy was determined by assessment of serum HCV RNA. Any adverse events during treatment were recorded.
**Results:** 2400 cirrhotic egyptian patients with chronic HCV infection treated with sofosbuvir and ribavirin for 24 weeks were enrolled in the study, their mean age (SD) was 53.9 + 6.5 years, 64.54% were males, they were all cirrhotics, 3.41% were treatment-experienced; baseline mean HCV RNA was 4.33 x $10^6$IU/ml. Overall, 94.37% completed the full course of therapy. Overall, SVR12 rates were 71.2%. The most common adverse events were fatigue, myalgia, headache, insomnia, and anemia. 135 patients stopped treatment permanently due to appearance of complications prevented continuation of treatment (44 cases with hepatic encephalopathy with sever elevated bilirubin and 91 cases with ascites).
**Conclusion:** Sofosbuvir and ribavirin is safe and effective treatment for HCV patients with liver cirrhosis. However, further studies are needed to establish the most optimal treatment regimen for this population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0045 TREATMENT OF HEPATITIS C INFECTION IN RENAL TRANSPLANT RECIPIENTS: A GOLDEN AGE

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**Introduction:** Infection by hepatitis C virus (HCV) in kidney transplant recipients is associated with an increased progression of hepatic fibrosis. Studies in kidney transplant patients demonstrate that HCV infection is associated with higher rates of rejection and increased risk of mortality. Causes directly related to HCV, such as glomerulonephritis and increased risk of diabetes may affect the outcome of the graft. At this moment, eradication of HCV infection with the direct-acting antivirals (DAAs) is feasible after kidney transplantation with few treatment-related side effects.
**Aims & Methods:** Objective: Analyse the effectiveness and safety of new therapeutic regimens in the treatment of HCV in kidney transplant recipients. Methods: Prospective cohort study of kidney transplant recipients with HCV infection undergoing treatment with the new DAAs. The primary endpoint was sustained virologic response at 12 weeks after completion of therapy (SVR12). The secondary endpoint was the treatment-related side effects.
**Results:** Thirteen kidney transplant recipients were included (69.2% male, mean age 55 ± 8 years) with HCV infection, with a median viral load at the time of treatment initiation of 6.65 log (IQR 3.99 – 7.43 log), proposed for 12 (n = 6) or 24 weeks (n = 7) of treatment with the following regimens (fourteen treatments in thirteen patients).

| | |
|---|---|
| Sofosbuvir + Ledipasvir | N = 8 |
| Sofosbuvir + Ribavirina | N = 3 |
| Sofosbuvir + Daclatasvir (±Ribavirina) | N = 2 |
| Ombitasvir-paritaprevir-ritonavir + Dasabuvir | N = 1 |

Nine (69.2%) patients were infected with genotype 1 (**33**.3% subtype 1 a) and 4 (30.8%) with genotype 3. Three had advanced fibrosis and five had cirrhosis. Three patients were previously treated with interferon. All patients had rapid virologic response (undetectable viremia at week 4 after starting DAA therapy). The eight patients who have completed follow-up up to 12 weeks post-treatment achieved SVR12 (100%).
At week 4 after completing DAA therapy, 9/9 patients obtained undetectable viremia. In all regimens with ribavirin it was necessary to reduce the dose and start erythropoietin. One patient suspended sofosbuvir + ribavirina due to severe anaemia and later was started on sofosbuvir + daclatasvir. A HCV genotype 1 a cirrhotic patient with had suspended the treatment (sofosbuvir + ledipavir) at week 5 due to septic shock (lower limb cellulitis) but SVR12 was still achieved. Serum levels of calcineurin inhibitors were monitored and adjusted to maintain therapeutic levels. Acute kidney injury by cyclosporin intoxication occurred in the patient undergoing treatment with Ombitasvir-paritaprevir-ritonavir + Dasabuvir, since the usual dose of the immunosuppressant was not reduced at the start of treatment. There has been no rejection of the graft during the study.
**Conclusion:** The new regimens with DAAs are associated with high rates of SVR in kidney transplant recipients and rare serious adverse events in a group historically difficult to treat.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0047 ROLE OF DIFFERENT CYTOKINE POLYMORPHISMS IN PREDICTING THE RESPONSE TO PEGYLATED INTERFERON ALFA-2A PLUS RIBAVIRIN IN EGYPTIAN CHILDREN WITH CHRONIC HEPATITIS C GENOTYPE 4

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**Introduction:** . The response to treatment in hepatitis C virus (HCV) infection varies between individuals. Whereas some variation may be attributable to viral and environmental variables, it is probable that host genetic background also

plays a significant role. It has been shown that cytokine genes are polymorphic, and some of these mutations may influence the production of cytokines and affect the host immune response in HCV infection. Information about treatment predictors, and even the response rates, in children with chronic hepatitis C (CHC), genotype 4 is limited.
**Aims & Methods:** The aim of this study was to investigate the ability of different factors including the genotype polymorphism of a panel of cytokines in predicting the response to Pegylated interferon (PEG-INF) and ribavirin (RBV) in a group of Egyptian children with CHC, genotype 4.
**Methods:** 57 children aged 5–17 years (48 males & 9 females) with previously untreated CHC, Genotype 4 were analyzed for single nucleotide polymorphisms of interleukin (IL) IL-28B, IL-10, IL-6, interferon-gamma (IFN- $\gamma$), tumor necrosis factor-alpha (TNF- $\alpha$), transforming growth factor-beta (TGF- $\beta$) by polymerase chain reaction using sequence-specific primers (PCR-SSP). They received a dose of PEG-INF alfa-2 a (Reiferon Retard®) equivalent to the dose licensed for adults based on calculated conversion to body surface area (BSA) {BSA/1.73 × 160ug/week} plus RBV (15 mg/kg/day) for 48 weeks. The primary end point was sustained virologic response (SVR). Pretreatment liver biopsy was done and evaluated using METAVIR fibrosis and activity scores.
**Results:** The majority of studied children (82.5%) have low baseline viral load (< 600, 000 IU/ml). Concerning fibrosis, 30 children had no fibrosis (F0), 21 had (F1) and only 6 had (F2). The frequencies of different dimorphic polymorphisms were as follows: IL-28B- 12979860 C/T 82.5%, C/C 12.2%, T/T 5.3%; IL-10-1082 G/G 40%, A/A 37.5%, G/A 22.5%; IL-10-819 C/T 47.5%, C/C 45%, T/T 7.5%; IL-10-592 C/C 55%, C/A 37.5, A/A 7.5%; IL-6-174 G/G 67.5%, G/C 17.5%, C/C 15%; IFN $\gamma$ + 874 T/A 40%, T/T 35%, A/A 25%; TNF-$\alpha$ G/G 72.5%, G/A 25%, A/A 2.5%; TGF-$\beta$ codon10 T/T 40%, T/C 35%, C/C 25%. Overall, SVR was attained by 71.9% (41/57) of all children with higher response rate in older chidren (> 11ys) [86.4 vs. 62.8% P = .05]. 77% of studied males attain SVR, versus 44% of females (p = .045). 87% of those with early virologic response (EVR) attained SVR (p = 0.000). AFs were generally mild or moderate in severity, primarily flu-like symptoms. Dose was modified because of hematological AFs in 24% of children. However, all children continued their treatment. SVR was not influenced by any of the studied cytokine polymorphism except for the polymorphism of IL-10-1082, where the G/A genotype which was significantly associated with bad response to treatment (p = 0.016). A multivariate logistic regression analysis showed that male sex, viral genotype 4 b and 4 e and achievement of EVR are independent predictors of SVR. No effect of other factors like viral load, duration of infection, presence of auto antibodies, high ALT levels, stage of fibrosis or degree of necroinflammatory activity was observed on SVR in this population infected with genotype 4.
**Conclusion:** Treatment with PEG-IFN alfa-2 a and RBV should be considered for children with CHC genotype 4 because it provides high response rates with improved tolerability and alleviates the long-term consequences of hepatitis C during adulthood when treatment is associated with additional negative prognostic factors.EVR, is a strong predictor of SVR in children as in adult. However, SVR in this population does not seem to be influenced by cytokine gene polymorphisms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0048 PERFORMANCE OF CONTRAST ENHANCED ULTRASOUND (CEUS) IN THE DIAGNOSTIC OF FOCAL LIVER LESIONS – MONOCENTRIC EXPERIENCE

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**Introduction:** Focal liver lesions (FLLs) are often found by ultrasonography in asymptomatic patients and also during follow-up in chronic liver diseases and in oncologic patients. In the last years CEUS is used more and more for FLLs' assessment considering that is non-irradiant, less expensive than sectional imaging and also that it can be used in patients with renal failure.
**Aims & Methods:** The aim of this study was to evaluate the diagnostic performance of contrast enhanced ultrasound (CEUS) in assessing FLLs in a large monocentric experience. The study included 721 patients (57.8% male, mean age 59.6 ± 13.1 years) with 874 FLLs (mean diameter of 4.5 ± 3.1 cm), which were first characterized by CEUS and then were finally evaluated by a 'gold-standard' method (contrast enhanced CT, contrast enhanced MRI or histology). The CEUS diagnosis was based on the FLLs' enhancement pattern following contrast bolus, according to the European Guidelines for the use of CEUS (1). Using the ''gold-standard'' methods, we calculated the sensitivity (Se), Specificity (Sp), and accuracy (Ac) of CEUS for the diagnostic of FLLs.
**Results:** From de 874 FLLs, CEUS was conclusive for the benign vs. malignant nature of the lesions in 776 (88.8%) cases. Using CT, MRI or histology, we established the final diagnostic of the lesions as follows: 246 (28.1%) hepatocellular carcinomas (HCC), 223 (25.5%) liver metastasis, 124 (14.2%) hemangiomas, 30 (3.4%) adenomas, 37 (4.2%) hepatic abscesses, 16 (1.9%) cholangiocarcinomas, 55 (6.3%) focal nodular hyperplasias (FNH), 36 (4.1%) regenerative nodules, 3.3% (29) focal fatty liver alterations (FFLA), 15 (1.8%) liver cysts, 38 (4.3%) other benign lesions, 25 (2.9%) other malignant lesions. For benign liver lesions, CEUS had 78.3% Se, 94.8% Sp, and 87.4% Ac. For the diagnostic of malignant lesions, CEUS had 82.9% Se, 86.4% Sp, and 84.2% Ac. For HCC, CEUS had a 65% Se, 91.4% Sp, and 81.8% Ac. For the diagnostic of liver metastases, CEUS had 74.4% Se, 93.2% Sp, and 86.7% Ac. For liver hemangiomas, CEUS achieved 73.3% Se, 95.6% Sp and 91.1% Ac. For FNH CEUS had 72.7% Se, a 97.3% Sp and a diagnostic Ac of 95%.
**Conclusion:** CEUS is a reliable diagnostic, being able to differentiate between malignant and benign lesions in 88.8% cases. The best accuracy was observed for diagnosing hemangiomas and FNHs (91 and 95%, respectively), and the lowest for HCCs (approximately 82%).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0049 TRANSIENT ELASTOGRAPHY FOR DIAGNOSIS OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION IN PATIENTS WITH ALCOHOL-RELATED LIVER CIRRHOSIS

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**Introduction:** Worldwide, up to 50% of liver cirrhosis is due to alcohol consumption [1]. Clinically significant portal hypertension (CSPH) is a main complication of liver cirrhosis. Hepatic venous pressure gradient (HVPG) measurement is the gold-standard method to assess the presence of CSPH, defined as HVPG ≥ 10 mmHg [2]. However, its use in clinical practice is limited as it is expensive and invasive. Esophageal varices are one of the first findings of CSPH. In patients with virus-related compensated cirrhosis, non-invasive methods are considered to rule-in EV, but the diagnostic value of transient elastography (TE) for EV in alcohol-related liver cirrhosis remains to be ascertained (Baveno VI consensus) [3].
**Aim:** To establish the diagnostic value of liver and spleen stiffness measurements in patients with compensated alcohol-related liver cirrhosis for diagnosis esophageal varices (EV).
**Methods:** 74 patients previously diagnosed with compensated liver cirrhosis due to alcohol intake (N = 26) and HCV infection (N = 48); 48% were males; mean age 50.9 years. All patients underwent TE measurements of both liver and spleen for the assessment of liver stiffness (LS) and spleen stiffness (SS) as well as abdominal ultrasonography measurements of the size of liver and spleen, upper endoscopy for EV assessment, and blood sampling. Statistical analysis was performed using nonparametric methods (Mann-Whitney u-test).
**Results:** In HCV-related liver cirrhosis, significant difference was observed in all parameters in patients with and without esophageal varices. Patients with EV had higher LS 27.9 (IQR 21–45) kPa vs 20.6 (IQR 16–26.2) kPa and SS 74.2 (IQR 52–75) kPa vs 38.6 (34–53.5) kPa than those without EV, as well as spleen diameter, platelet count ($p < 0.05$). However, no statistically significant difference of LS, SS, or spleen diameter was observed in patients with alcohol-related liver cirrhosis according to presence of EV. Moreover patients with alcoholic liver cirrhosis but without EV had significantly higher median of platelet counts $210*10^9$/ml (IQR 192–350) vs 98 (IQR 76–153) than those with EV and the same etiology of liver cirrhosis.
**Conclusion:** TE of liver and spleen is a non-invasive tool for diagnosis of EV in HCV-related liver cirrhosis. However, this finding could not be applied for liver cirrhosis due to other etiologies (e.g. alcohol-related). No correlation between spleen size and stiffness was found in alcohol-related liver cirrhosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0050 A NEW ULTRASOUND-BASED METHOD TO DETECT LIVER STEATOSIS USING CT AS REFERENCE STANDARD

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**Introduction:** Steatosis is the most common liver disease in developed countries, being related to other disorders such as diabetes and metabolic syndrome. Biopsy represents the standard of reference in diagnosis steatosis, but it is an invasive technique. As a non-invasive option, CT measurements on liver and spleen may be used, with a 0.9 threshold on their ratio being proven as diagnostic.
**Aims & Methods:** Our aim was to develop a new method based on ultrasound measurements in the liver and the right kidney allowing to detect steatosis using the CT method as reference standard. We retrospectively reviewed images of patients who performed both ultrasound and CT within 10 days. For each patient, we measured CT density of both liver and spleen by placing a region of interest (ROI) of 100 pixel in the same slice; the liver:spleen ratio was calculated. Similarly, measurements on both liver and right kidney in a single ultrasound image were obtained using ImageJ software (Java; developed by the National Institute of Health); the kidney:liver ratio was calculated. The correlation between ratios obtained on CT and ultrasound was estimated using the Spearman correlation coefficient, while the diagnostic performance of the new method based on ultrasound was calculated using ROC analysis. Patients with a CT ratio $< 0.9$ were considered as affected by steatosis. Thresholds were given for nearly-95% sensitivity or nearly-95% specificity.
**Results:** A total of 45 patients [median age 56 years (IQR 50–74 years)] were analyzed, 14 (31%) having steatosis according to CT ratio. The median CT ratio was 1.10 (IQR 0.87 –1.24), while the ultrasound ratio distribution was 0.98 (0.82 –1.13). The correlation between the two ratios was 0.524 ($P < .001$). At ROC analysis, AUC was 0.840. Thresholds for nearly-95% sensitivity and nearly-95% specificity were 1.16 (25% specificity) and 0.75 (50% sensitivity), respectively.
**Conclusion:** We developed a new ultrasound-based method to rule out liver steatosis showing a high diagnostic performance. After validation, patients with a right kidney:liver ratio (measured with this method) higher than 1.16 may avoid biopsy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0051 NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS BY MEANS OF TRANSIENT ELASTOGRAPHY AND FIBROTEST IN PATIENTS WITH HCV COMPENSATED LIVER CIRRHOSIS

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**Introduction:** The severity of liver disease should be assessed prior to therapy. Noninvasive evaluation of liver fibrosis can be performed using biological test like FibroTest or by using ultrasound based elastographic methods like Transient Elastography (TE).
**Aims & Methods:** The aim of the study was to evaluate the accuracy of these tests (FibroTest and TE) for predicting HCV liver cirrhosis (LC), in naïve or treatment-experienced patients, with compensated liver disease.
**Patients and methods:** The study included 206 consecutive patients previously diagnosed with compensated HCV LC based on clinical, biologic, ultrasonographic, morphologic, laparoscopic or endoscopic (esophageal varices) criterias, who were considered for interferon free treatment (Viekirax/Exviera). Liver fibrosis was assessed during a two week period by means of TE (using M or XL probe) and by FibroTest. For TE reliable measurements were defined as median value of 10 liver stiffness measurements, with a SR $\geq 60\%$ and an IQR $< 30\%$. For diagnosing cirrhosis by means of TE we used a cut-off value 12.5 kPa [1] and for FibroTest a value of 0.75.
**Results:** Out of 206 patients, reliable measurements by TE were obtained in 89.8%, so that the final analysis included 194 patients (having valid TE and FibroTest). According to FibroTest cut-off, 74.2% (144/194) patients were correctly classified, while according to TE cut-off – 92.3% (179/194) patients ($p < 0.0001$). Out of the 194 cirrhotics, 2.1% were misclassified by TE as having significant fibrosis (F2) and 6.2% with severe fibrosis (F3). When we evaluated the performance of FibroTest, 5.7% of patients with LC were misclassified as having F2, 16.5% as having F3 and 2.6% as having F3/F4, 1% as having F1-F2.14% (7/50) patients misclassified by FibroTest had grade I esophageal varices and 2% (1/50) had grade II esophageal varices.
**Conclusion:** The accuracy of FibroTest for predicting HCV liver cirrhosis in naïve or treatment-experienced patients, with compensated liver disease was significantly lower than of TE (74.2% vs. 92.3%; $p < 0.0001$).
**Disclosure of Interest:** I. Sporea: Ioan Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric.
A. Popescu: Alina Popescu received speaker fees from Philips.
R.L.D. Sirli: Roxana Şirli received speaker fees from Philips.
All other authors have declared no conflicts of interest.

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## P0052 THE VALUE OF ELASTPQ FOR THE EVALUATION OF LIVER STIFFNESS IN PATIENTS WITH B AND C CHRONIC HEPATOPATHIES

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**Introduction:** Accurate staging of liver fibrosis is highly important for patients with chronic liver diseases for treatment, prognosis and for long-term follow-up. Transient Elastography-TE (Fibroscan; Echosens, Paris, France), the first and the most widely used method for liver stiffness assessment, is the only ultrasound-based elastographic technique validated and recommended in some guidelines for diagnosis and management of patients with chronic liver disease [1, 2].
**Aims & Methods:** The aim of this study was to evaluate the diagnostic performance of a point shear wave elastography using ARFI technique - ElastPQ, in patients with B and C chronic hepatopathies, using Transient Elastography (TE) as the reference method, since it is a validated method for liver fibrosis assessment [1, 2]. .
**Subjects and methods:** The study included 228 consecutive subjects with chronic hepatopathies (26% HBV, 74% HCV) from whom 51% had liver cirrhosis. Liver stiffness (LS) was evaluated in the same session by means of 2 elastographic methods: TE (Fibroscan, Echosens) and ElastPQ (Philips, Affinity) techniques. Reliable LS measurements were defined as follows: for TE – the median value of 10 LS measurements with a success rate $\geq 60\%$ and an interquartile range $< 30\%$. For ElastPQ – the median value of 10 LS measurements in the liver parenchyma, at least 1 cm below the capsule, avoiding large vessels. For TE M and XL probes were used. For differentiating between stages of liver fibrosis we used the following cut-off values for TE [3]: mild fibrosis ($F \geq 1$)-6.1 kPa, significant fibrosis ($F \geq 2$)-7.2 kPa, severe fibrosis ($F \geq 3$)-9.6 kPa and for liver cirrhosis ($F = 4$)-14.5 kPa.
**Results:** Reliable liver stiffness measurements were obtained in 90.7% (207/228) by means of TE and in 98.7% (225/228) with ElastPQ. In the final analysis 205 patients were included. The ElastPQ values ranged from 2.32 to 44.07 kPa (median = 10.42 kPa). Based on TE cut-off values [3] we divided our cohort into 4 groups: F1: 62/205 (30.2%); F2: 14/205 (6.8%); F3: 32/205 (15.6%); $F = 4$: 97/205 (47.4%). The areas under the receiver operating characteristic curve were: 0.903 for patients with mild fibrosis ($F \geq 1$), 0.953 for moderate fibrosis ($F \geq 2$), 0.967for severe fibrosis ($F \geq 3$) and 0.947 for cirrhosis ($F = 4$). The best cut-off values for discriminating mild, moderate, severe fibrosis and cirrhosis were 6.4, 7.2, 8.5 and 9.9 kPa, respectively. In our cohort there was a very good correlation between measurements obtained by Transient Elastography and ElastPQ ($r = 0.85$, $p < 0.001$).
**Conclusion:** ElastPQ is a method that seems to be good for the diagnosis of all stages of liver fibrosis in patients with chronic hepatopathies, with good diagnostic accuracy.
**Disclosure of Interest:** I. Sporea: Ioan Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric.
R.L.D. Sirli: Roxana Şirli received speaker fees from Philips.
A. Popescu: Alina Popescu received speaker fees from Philips.
All other authors have declared no conflicts of interest.

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## P0054 ROLE OF LOW MOLECULAR WEIGHT HEPARINS (LMWH) IN PREVENTION OF THROMBOEMBOLIC COMPLICATION AFTER TRANSARTERIAL CHEMOEMBOLIZATION (TACE) IN HEPATOCELLULAR CARCINOMA

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**Introduction:** Portal vein thrombosis is a common complication after Transarterial Chemoembolization (TACE) in Hepatocellular Carcinoma (HCC) because HCC may be highly vascular with significant arteriovenous shunting, both into the portal venous system and hepatic venous system.

**Aims & Methods:** This is the first clinical trial to evaluate the role of low molecular weight heparins (LMWH) with TACE in HCC for prevention of thromboembolism complications (portal vein thrombosis). This study was conducted on 40 patients with HCC requiring Transarterial chemoembolization who presented to the Tropical Medicine Department Tanta University and Interventional Radiology Department of Ain Shams University Hospitals starting from April 2015. Patients were divided in two groups: Group I included 20 patients with HCC treated by TACE only. Group II included 20 patients with HCC treated by TACE and adjuvant dose of LMWH. Radiological Assessment of efficacy of procedure and detection of portal vein thrombosis as a complication was done using ultrasound abdomen and pelvis and triphasic spiral CT with contrast.

**Results:** This study was conducted on 40 patients with HCC requiring Transarterial chemoembolization who presented to the Tropical Medicine Department Tanta University and Interventional Radiology; their age ranged between 43 to 74 years, 28 males and 12 female, 26 patients (65%) were child A and 14 patients (35%) were child B. Right hypochondrial pain was the most frequent symptom, 37 patients (92.5%) were seropositive to HCV and 3 patients (7.5%) were HBsAg positive. The tumor was single in 45% of patients, two nodules in 37% and three nodules in 18% of patients with AFP more than 400 ng|ml in 60% of patients. In 57% of patients tumors were located in the right lobe and portal vein was patent in all patients before the procedure The incidence of portal vein thrombosis after TACE was more in group I than group II with Seven cases in group I & only one case in group II.

**Conclusion**: LMWH with TACE in hepatocellular carcinoma is strongly recommended for prevention of thromboembolism complications (portal vein thrombosis). However, larger randomized controlled studies are needed to confirm these obvious findings.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0055 DRUG-ELUTING BEADS VERSUS CONVENTIONAL CHEMOEMBOLIZATION FOR THE TREATMENT OF UNRESECTABLE HEPATOCELLULAR CARCINOMA: A META-ANALYSIS

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**Introduction: Background:** Despite the promising results of earlier studies, a clear superiority of drug-eluting beads transarterial chemoembolization over conventional chemoembolization in unresectable hepatocellular carcinoma patients has not been established yet.

**Aims & Methods:** To evaluate the efficacy and safety of the two treatments in unresectable hepatocellular carcinoma patients computerized bibliographic search on the main databases was performed. One-year, two-year, three-year survival rates were analyzed. Hazard ratios from Kaplan-Meier curves were extracted in order to perform an unbiased comparison of survival estimates. Objective response and severe adverse event rate were analyzed too.

**Results:** Four randomized-controlled trials and 8 observational studies with 1449 patients were included in the meta-analysis. Non-significant trends in favor of drug-eluting beads chemoembolization were observed as for 1-year (odds ratio: 0.76, 0.48–1.21, $p = 0.25$), 2-year (odds ratio: 0.68, 0.42–1.12, $p = 0.13$) and 3-year survival (odds ratio: 0.57, 0.32–1.01, $p = 0.06$). Meta-analysis of plotted hazard ratios confirmed this trend (hazard ratio: 0.86, 0.71–1.03, $p = 0.10$). Pooled data of objective response showed no significant difference between the two treatments (odds ratio: 1.21, 0.69–2.12, $p = 0.51$). No statistically significant difference in adverse events was registered (odds ratio: 0.85, 0.60–1.20, $p = 0.36$).

**Conclusion:** Our results stand for a non-superiority of drug-eluting beads chemoembolization with respect to conventional chemoembolization in hepatocarcinoma patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0056 EFFICACY OF LOW-DOSE CAPECITABINE AND SORAFENIB IN PATIENTS WITH ADVANCED ALFA-FETOPROTEIN SECRETING HEPATOCELLULAR CARCINOMA: A ONE-YEAR EXPERIENCE

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**Introduction:** The continued appearance of new cases of hepatocellular carcinoma (HCC) with horribly increasing incidence makes it the fifth common worldwide solid tumor; unfortunately, most of the cases present in advanced or inoperable stage. In Egypt, the majority of patients are due to HCV, and actually, they are presenting late with reduced median survival, and therapy in most cases is palliative. The treatment options either curative in the form of hepatic resection or liver transplantation and palliative to include transcatheter arterial chemoembolization (TACE) which is associated with partial response in 10–55%, radioembolization, and medical therapy with sorafenib which is an oral multikinase inhibitor that had led to significant lengthening of short term-survival when compared to placebo. The increasing number of patients presented with advanced HCC with no other eligible treatment options that can be offered for them as surgery, local ablative therapies or chemoembolization will put us in a challenging situation.

**Aims & Methods:** Evaluation of the efficacy of low-dose capecitabine combined with sorafenib which are potentially safe and effective drugs based on previous studies, in subset of Egyptian HCV patients presented with advanced HCC who were unfit for surgical or locoregional therapies. 15 patients with advanced HCC, unfit for surgical or locoregional intervention, with PS $< 2$ recieved Capecitabine 500 mg/day with sorafeneb 200 mg twice daily till normalization of AFP then the treatment was modified to capecitabine 250 mg every other day and sorafenib 400 mg once daily. They were followed every 3 months for size, number of focal masses and AFP. 30 patients were selected as control group, they received supportive therapy ($n = 15$) or sorafenib only ($n = 15$).

**Results:** After 10 months of therapy, 6 patients showed complete response (40%) with complete recanalization of portal vein ($n = 2$) and treatment was stopped and the others showed partial portal vein recanalization so treatment is continued till now. 1 patient (6.7%) showed recurrence of the disease and died after one month, 8 patients showed partial response (53.3%) and still on treatment. The control groups showed a highly significant reduction in survival when compared to patients who received capecitabine and sorafenib ($12.9 \pm 2.1$, $7.9 \pm 0.9$, $4.5 \pm 1.3$ months, $p = 0.000$).

**Conclusion:** Combined low-dose capecitabine and sorafenib proved to be safe with low toxicity profile and deserves further attention as a convenient, outpatient-based chemotherapy regimen in patients with advanced HCC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0057 CHANGING PATTERN IN ETIOLOGIC FACTORS OF HEPATOCELLULAR CARCINOMA IN LEBANON

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**Introduction:** HCC is a world-leading cause of mortality with HBV being its major etiologic factor and a worldwide geographic distribution similar to that of HBV. Previous data from Lebanon identified HBV in 51% of cirrhosis and 48% of HCC. The prevalence of HBV infections in Lebanon is decreasing in relation to vaccination, and preventive measures.
**Aims & Methods:** We aimed at studying the etiologic changes in HCC, and the prognostic implications. We compared two periods 1999–2005 (90 consecutive patients), and 2006–2015 (88 patients).
**Results:** Patients were males in respectively 85 and 78%. The etiology showed a stable prevalence of alcohol and HCV related liver disease, whereas we noted a decrease in HBV from 54 (62%) to 43 (48.9%), and an increase in Idiopathic/NAFLD from 10 (10.9%) to 17 (27.3%). Although we noted no differences in terms of severity of underlying liver disease or characteristics of the tumors, HCC occurred in the absence of cirrhosis in 14.8% in 2007–2015 as compared to 2.2% in the previous period ($p = 0.007$). The eligibility for a curative treatment increased from 21.1% to 35.2% ($p = 0.013$). We noted no difference in survival based on time periods with the exception of a better survival in the newer period for patients undergoing a curative resection or ablative therapy.
**Conclusion:** In conclusion we note that we have a changing etiologic epidemiology of HCC in Lebanon, with HBV decreasing, a steady HCV and an increase in the incidence of NAFLD related HCC. These results highlight the positive impact of our national hepatitis program for vaccination, screening, and treatment in decreasing the incidence of HBV and later HCV.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0058 HEPATIC RESECTION IS SUPERIOR TO TACE AND PERCUTANEOUS ABLATION IN B1-B2 SUBGROUPS OF PATIENTS WITH INTERMEDIATE STAGE HEPATOCELLULAR CARCINOMA

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**Introduction:** In hepatocellular carcinoma **(HCC)** the intermediate BCLC stage (BCLC-B stage) is characterized by a high clinical heterogeneity. For a tailored treatment, in 2012 it was suggested that the BCLC-B stage should be divided into 4 sub-stages according to the tumour burden (IN or OUT the Up-to-seven criterion) and the Child-Pugh scores (A5 to B9). In B1-B2 stages hepatic resection (HR), percutaneous ablation (PA) and transarterial chemoembolization (TACE) are the proposed treatment.
**Aims & Methods:** To investigate the efficacy of the above mentioned treatments in term of survival in a Romanian cohort of BCLC – B patients with HCC.
**Methods:** Treatment indications for 200 newly diagnosed HCC patients BCLC-B stage referred to our service between 01.2009–01.2014 were analysed retrospectively. Patients were grouped according to the proposed BCLC–B sub-classification model. Baseline patient and tumour characteristics, therapy options and overall survival (OS) were analysed for the B1-B2 subgroups.
**Results:** Of the 200 patients with BCLB B 151 were in B1 + B2 substages, 42 (27.8%) in B1 and 109 (72.2%) in B2. HR was used in 46 pts (23%), 23 in B1 (54.7%) and 23 in B2 (21%), PA in 13 cases, 5 in B1 (11%) and 8 in B2 (7.9%) and TACE in 16 patients, 7 in B1 (16.6%) and 9 in B2 (8.25%). Sorafenib was used in 35 (32%) B2 patients. Patients treated by HR had larger tumors but better liver function. In the B1 + B2 group patients treated by HR had a significantly higher median survival (47 months) in comparison with thosed treated by PA (22 months), TACE (25 months) but also sorafenib (27 months) (p-value for linear trend: $< 0.001$). B1 patients treated with HR had a better median survival (47 months) compared with those treated with: PA (27 months, $p = 0.017$), TACE (26 months, $p = 0.33$) or BSC (16 months, $p < 0.001$). The 1, 3, 5-year survival rates were 81%, 47%, 7% for HR; 64%, 32% and 0% for TACE; 52%, 0%, 0% for PA; and 0%, 0%, 0% for BSC respectively. HR was superior in terms of survival also in B2 patients (46 months median survival) when comparing to TACE (24 months, $p < 0.05$), PA (10 months, $p < 0.001$), Sorafenib (27 months, $p = 0.117$) or BSC (10 months, $p < 0.000$). The 1, -3, -5-year survival rates were 71%, 42%, 7% for HR; 51%, 0% and 0% for TACE; 50%, 0%, 0% for PA; 59%, 0%, 0% for Sorafenib; and 0%, 0%, 0% for BSC respectively. The perinterventional overall 1-month mortality was higher in HR group (4.34%) in comparison with TACE (0%) and PA (0%). The mortality was higher in B2 resected patients (8.9%) in comparison to B1 (0%) but without statistical significance ($p = 0.15$).
**Conclusion:** In our cohort of patients, hepatic resection was used as curative treatment in 23% of patients included in the B1 and B2 sub-stage. In this group of patients HR provided a significant longer survival in comparison to TACE and PA. To decrease the perinterventional mortality a proper selection of patients with careful attention to liver function, degree of portal hypertension and coagulation is mandatory.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0059 PROGNOSIS OF EARLY STAGE HEPATOCELLULAR CARCINOMA SHOWING COMPLETE RESPONSE AFTER FIRST TRANSARTERIAL CHEMOEMBOLIZATION: A ROLE OF SCHEDULED SECOND TACE

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**Introduction:** Transarterial chemoembolization (TACE) is performed with curative intent in some patients with early stage hepatocellular carcinoma (HCC) in real clinical practice. As radiological complete response (CR) after TACE does not always match histological total necrosis, scheduled second TACE has been tried for early stage tumor with complete response after first TACE, which lacks sufficient supporting data.
**Aims & Methods:** A total of 178 patients with early stage HCC, defined by Barcelona Clinic Liver Cancer stage (BCLC) 0 or A, who were initially treated with TACE and showed CR by mRECIST criteria at one month follow-up computed tomography (CT) were analyzed. Among them, 90 patients received scheduled second TACE in absence of viable tumor at one month follow-up CT, while 88 patients were monitored without TACE until viable lesions are detected (on-demand approach).
**Results:** During a median 4.6 years of follow-up (range: 0.4 – 8.8 years), mortality was observed in 71 patients (39.9%), with a 5-year survival rate of 60.4%. Overall and local tumor recurrence was observed in 135 (75.8%) and 103 (57.9%) patients. The overall and local recurrence-free survival rate at 1 year was 44.4% and 56.2%. In multivariable model, treatment strategy (scheduled second TACE vs. on-demand) was independent factor associated with survival [hazard ratio (HR) (95% confidence interval (CI)): 0.56 (0.34–0.93), $p = 0.025$], along with underlying liver disease, Child-Pugh class, and BCLC stage. BCLC stage was more advanced for those who received scheduled second TACE. When stratified according to the BCLC stage, scheduled second TACE was associated with favorable overall survival rate (62.1% vs. 39.1% at 5-years) and local recurrence free survival rate (31.9% vs. 10.5% at 2-years) in BCLC stage A patients, but not in BCLC 0 patients.
**Conclusion:** Scheduled second TACE was associated with better survival and lower local recurrence rate for BCLC A stage tumor showing CR after initial TACE. Scheduled second TACE strategy may play a significant role for this subset of early-stage HCC patients, which warrants further validation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0060 HEPATIC VENO-OCCLUSIVE DISEASE (VOD) AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN PEDIATRIC PATIENTS: ROLE OF LIVER STIFFNESSS

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**Introduction:** VOD is a clinical syndrome characterized by hepatomegaly, ascites, weight gain and jaundice which can develop more frequently in the first 30 days after HSCT and that is associated with >80% mortality. Incidence has been estimated to be 13.7% (range 0%–62.3%). In this syndrome, sinusoidal endothelial cells and hepatocytes in the zone 3 of the hepatic acinus are damaged by toxic metabolites generated during the conditioning regimen leading to post-sinusoidal portal hypertension (PH) that dominates clinical conditions. To date, VOD diagnosis is based primarily on established clinical criteria (modified Seattle or Baltimore criteria) and no predictive factor are known. Liver stiffness measurement (LSM) by Fibroscan® is a safe, accurate and non invasive method used to better identify liver fibrosis and PH degree in chronic liver disease patients.
**Aims & Methods:** The aim of our study is to verify the role of LSM by Fibroscan® in predicting VOD development in a pediatric population who underwent HSCT. We prospectively included all patients with hemato-oncologic disease with indication for allo and auto-HSCT who underwent total-body irradiation (TBI) or busulfan-based conditioning regimen, referred to our Hemato-Oncologic Pediatric Unit of Sant'Orsola Hospital from November 2014 to April 2016. At enrollment (before pre-HSCT chemotherapy) all patients underwent laboratory tests, routine abdomen ultrasonography examination (US) and LSM. Subsequently laboratory tests and LSM were performed at 7–10 days (T1), 17–20 days (T2) and 27–30 days (T3) after transplantation. All examinations were conducted bedside for minimizing infection risks.
**Results:** Overall 20 pediatric patients (14 males, 6 females, mean age: 137 months, min. 54, max 245) were enrolled; 4 patients (20%) of studied population developed VOD. No evident differences were observed at baseline LSM between patients who developed VOD and those who did not. LSM values sudden increased in the measurement made before VOD diagnosis and these values were also different from baseline and from previous one.
**Conclusion:** Our data show that the increase in LSM values seems to predict VOD development in patients who underwent HSCT. In fact, LSM values suddenly increased, respect to the previous measurement, some days before the onset of the disease, in absence of altered laboratory tests or clinical symptoms suggestive of VOD disease. According to the relevance of early diagnosis on clinical outcome, further studies are needed to confirm the predictive role of liver stiffness measurement for an early VOD diagnosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0061 DIFFERENT METHODS HANDLING COMMON BILE DUCT STONES WITH PERIAMPULLARY DIVERTICULA: THE EXPERIENCE COMPARISON BETWEEN TWO CENTERS FROM CHINA AND JAPAN

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**Introduction:** Periampullary diverticula (PAD) is known to be associated with an increased frequency of pancreatobiliary diseases [1]. Our previous study has demonstrated that PAD is an important factor for the occurrence and recurrence of common bile duct (CBD) stones [2]. It is widely accepted that the presence of PAD can be a technical obstacle to cannulation and requires skillful endoscopy manipulation [3–4]. Nevertheless, there has been little study about large scale appraisal of therapeutic effectiveness and safety of endoscopic retrograde cholangiopancreatography (ERCP) procedure when CBD stones combined with PAD.
**Aims & Methods:** This study was to investigate the optimal ERCP method for common bile duct stones combined with periampullary diverticula. Retrospective analysis of the first session therapeutic ERCP cases including two endoscopy centers (The first hospital of Lanzhou University, Gansu, China and Kyoto Second Red Cross Hospipal, Japan) between January 2012 and January 2015. Clinical data of all cases include the following properities: gender, age, with or without PAD, whether or not there was difficulty to remove stones, residual rate of CBD stone, post-ERCP complication. ERCPs were performed by experienced endoscopists who performed over 200 biliary interventions per year. Group of EST plus papillary balloon dilation was conducted at The First Hospital of Lanzhou University, a teaching hospital of Gansu in China. EST group was performed at Kyoto Second Red Cross Hospipal in China. Patients were placed under conscious sedation with meperidine and midazolam.
**Results:** A total of 3.196 (2, 309 Chinese, 887 Japanese) therapeutic ERCPs were enrolled in the final analysis. Of this total, 1, 491 patients (1, 259 Chinese, 232 Japanese) had CBD stones without PAD and 612 patients (459 Chinese, 153 Japanese) had CBD stones with PAD. In all of the data, there were no statistically significant between sex, but patients with PAD were significantly older than those without PAD ($67.61 \pm 13.51$ vs $60.85 \pm 16.82$, $P < 0.0001$). Whether from Chinese, or from Japanese, the rate of CBD stone with PAD was significantly higher than CBD stone without PAD (79.14% vs 72.82%, $P = 0.0025$; 68.61% vs 34.94%, $P < 0.0001$, respectively). Compared with EST, both the rate of difficulty to remove out stones and residue of CBD stones were significantly lower in EST plus EPBD than in EST (74.51% vs 32.46%, $P < 0.0001$; 27.45% vs 8.16%, $P < 0.0001$; respectively) on condition that CBD stones combined with PAD, but the post-ERCP complications had no significant difference between EST and EST plus EPBD (7.17% vs 13.38%, $P = 0.05$) (Table 1).

**Table 1:** Out-come of different ERCP methods for CBD stones with PAD between two groups.

| Index | EST plus EPBD group (The first hospital of Lanzhou University) | EST group (Kyoto Second Red Cross Hospital) | Chi-square | P value |
|---|---|---|---|---|
| Rate of difficulty to remove stone (n, %) | 124 (32.46) | 114 (74.51) | 78.2146 | <0.0001 |
| Rate of residual stone (n, %) | 28 (8.16) | 42 (27.45) | 32.4729 | <0.0001 |
| Rate of post-ERCP Complication (n, %) | 19 (13.38) | 16 (7.17) | 3.8534 | 0.0496 |

**Conclusion:** EST plus papillary balloon dilation was an optimal ERCP procedure for common bile duct stones in patients with periampullary diverticula.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0062 URSODEOXYCHOLIC ACID REDUCE THE WEIGHT GAIN VIA MODULATING THE COMPOSITION OF GUT MICROBIOTA

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**Introduction:** The accumulating evidence strongly suggests that the gut microbiota play an important role in the regulation of energy balance and weight in mammals and may influence the progression of obesity. (1) On the other hand, it is well known that bile acids are the most important regulators of the gut microbiome. (2) Together, these might suggest that pharmacological alteration of bile acid composition can modify the gut microbiota and thus, can provide the relevant therapeutic avenue for obesity and other metabolic disorders.
**Aims & Methods:** We investigated whether the ursodeoxycholic acid (UDCA), a commonly used therapeutic agent for the hepatobiliary disorders, can reduce the weight gain. Furthermore, we also demonstrated the effects of UDCA on the intestinal dominance of Firmicutes, which is known as a condition prone to obesity. The 6 weeks-old male Sprague Dawley (SD) rats were divided into 3 groups: the U10 (a group intraorally administered with 10 mg/kg UDCA), the U15 (a group with 15 mg/kg UDCA) and the control (a group with a saline as a vehicle). During a total of 3 weeks-administration of UDCA, a time course of lipid-related serological parameters e.g., triglycerides (TG), total cholesterol (TCH), and high-density lipoprotein (HDL) and a body weight were analyzed. To investigate the modulating effects of UDCA on the ratio of Firmicutes to Bacteroides, quantitative polymerase chain reaction (qPCR) methods using rat fecal materials were fulfilled after 3 weeks-administration of UDCA.
**Results:** The weight gain of U10 and U15 were significantly reduced compared with that of control and these were dose- and time-dependent manner. Using qPCR, we revealed the ratio of Firmicutes to Bacteroides in fecal materials of U10 and U15 were significantly reduced than that of control after 3 weeks-administration of UDCA. Finally, we demonstrated that the serum level of TG and TCH were decreased, whereas the level of HDL was elevated in U10 and U15 at all time point of experiment and these were also dose-dependent.
**Conclusion:** Taken together, we suggest that UDCA can reduce weight gain via preventing the intestinal dominance of Firmicutes. To address the possible mechanism for these alterations in composition of gut microbiota, further investigation might be needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0063 GENETIC POLYMORPHISMS OF IL-4 (C-590T), TNF-A (G-308A), PRSS1 (R122H) AND CFTR (DELF508C) GENES IN PATIENTS WITH ACUTE PANCREATITIS AND CHOLESTATIC SYNDROME

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**Introduction:** Acute pancreatitis is a multifactorial pathology with possible involving of genetic factors. Pancreatitis itself has strong and diverse impact on digestive system. Acute pancreatic inflammation frequently leads to cholestasis, though prediction of this complication remains tricky. There are multiple studies of the candidate genes' polymorphisms for acute and exacerbated chronic pancreatitis, depicting its understanding as a multifactorial pathology involving genetic factors. But the role of immune system, especially polymorphism of genes that regulate the inflammatory response in the pathogenesis of biliary/pancreatic inflammation is often left beyond attention. Study of different genetic polymorphisms may create a strong background for individualized therapies of biliary disorders.
**Aims & Methods:** The aim of the study is to find changes of biochemical parameters of cholestasis syndrome in patients with acute non-necrotizing pancreatitis, depending on the polymorphism of genes of interleukin 4 (IL-4, (C-590T), TNF-$\alpha$ (G-308A), PRSS1 (R122H) and CFTR (delF508C), etiologic factor and gender. Genetic studies performed for 101 patients, among them 19 (18.8%) were women and 82 (81.2%) men. There were 64 (63.37%) patients with alcoholic pancreatitis genesis (AGP) and 37 (36.63%) – with biliary (BGP). The genotypes distribution among examined patients and healthy people for the selected genes has been determined. The possible associative links of indicated genes polymorphism with the increased activity of gamma-glutamyl transferase, alkaline phosphatase, bilirubin and its fractions levels, the etiology of disease (alcoholic or biliary) and gender have been searched for.
**Results:** Distribution of genotypes among examined patients and healthy people was as follows: the PRSS1 (R122H) gene in all groups was represented by GG-genotype (100%); CFTR (delF508) gene – in 3 persons with NM-genotype (2.97%) and 98 with NN-genotype (97.03%); in control group of healthy people were registered only NN carriers; TNF-$\alpha$ (G-308A) gene: 81.19% with GG-genotype and 18.81% GA-genotype; the IL-4 (C-590T) gene among patients was represented in 58 (57.43%) patients by CC-genotype, in 34 (33.66%) – by CT-genotype, in 9 (8.91%) – by mutation TT-genotype, among healthy – in 26 (65%), 11 (27.5%) and 3 (7.5%), respectively ($\chi^2 < 1.0$, $p > 0.05$).
**Conclusion:** This study does not establish clear association of polymorphisms of PRSS1 (R122H), CFTR (delF508) and TNF-$\alpha$ (G-308A) genes with the increased activity of cholestatic syndrome, pancreatitis etiology and gender. However, the activity of cholestasis syndrome was higher, mainly in carriers of the TT-genotype of IL-4 gene (rs 2243250) and was characterized by 1.9 and 1.58 times growth of the gamma-glutamyl transferase (with biliary genesis) and 2.06 and 1.53 times (among women), total bilirubin - 1.85 and 2.13 times (with alcoholic genesis) and 1.66 and 1.87 times (among men), direct bilirubin - 2.81 and 3.22 times (with alcoholic genesis) and 2.47 and 2.96 times (among men) compared to the C-allele carriers, respectively.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0064 DURABLE RESPONSE IN THE MARKERS OF CHOLESTASIS THROUGH 18 MONTHS OF OPEN-LABEL LONG-TERM SAFETY EXTENSION STUDY OF OBETICHOLIC ACID IN PRIMARY BILIARY CIRRHOSIS

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**Introduction:** Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor (FXR) agonist developed for treatment of primary biliary cirrhosis (PBC). 216 patients were randomized and dosed in a double-blind (DB), placebo-controlled, phase 3 PBC trial (POISE); 198 patients completed the DB phase of the trial and 193 (97%) patients enrolled in the open-label long-term safety extension (LTSE).
**Aims & Methods:** The LTSE aim is to assess the continued durability of OCA on the markers of cholestasis and safety. Inclusion criteria for the DB phase: PBC diagnosis, ALP $\geq$ 1.67x ULN and/or total bilirubin > ULN to <2x ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, patients were randomized to: daily Placebo (PBO), 5 to 10 mg OCA titration group (titration after 6 months based on response/tolerability), or 10 mg OCA. In the LTSE, all patients were to be initially treated with 5 mg OCA regardless of DB treatment with the option to increase OCA dose up to 10 mg after 3 months. This analysis focuses on patients receiving $\leq$10 mg OCA daily. The LTSE phase is currently in progress with 170 total patients completing through 18 months (PBO, n = 41; Titration OCA; n = 45; 10 mg OCA, n = 50; all for patients receiving $\leq$10 mg OCA daily). LTSE demographics: mean age 56 y; female: 91%; white 94%.
**Results:** All OCA groups had significant reductions in ALP, GGT, ALT and AST (Table 1) after 12 months of treatment. In OCA Titration and 10 mg groups, this response was durable through an additional 18 months of the LTSE. For PBO, mean bilirubin increased during the DB period. OCA Titration and 10 mg groups sustained no increase in mean bilirubin in the DB or LTSE. Overall OCA was safe and well-tolerated; pruritus was the most common adverse event (AE) associated with OCA. Patients on OCA in the DB period showed a decrease in crude incidence of pruritus in the LTSE, from 56–68% (12 months DB treatment) to 19–36% (ongoing LTSE treatment). PBO subjects who initiated OCA in the LTSE saw an increase in pruritus consistent with initiation of OCA. While receiving OCA, initial changes in lipoprotein levels were sustained throughout the LTSE. Unrelated to OCA, 1 patient died as a result of sepsis secondary to endocarditis after a prosthetic aortic valve replacement.

**Table 1:** Laboratory changes through the double-blind and LTSE study period.

| Original Treatment Group | Placebo | OCA Titration | 10 mg OCA |
|---|---|---|---|
| **ALP (U/L)** | | | |
| DB Baseline | 310.3 (96.8) | 314.7 (122.1) | 307.7 (97.8) |
| Δ DB 12 mo | -12.1 (80.4) | -106.1 (87.0)*** | -122.0 (74.9)*** |
| Δ LTSE 18 mo | -97.8 (69.6)*** | -111.3 (90.3)*** | -106.8 (91.4)*** |
| **Bilirubin (μmol/L)** | | | |
| DB Baseline | 11.0 (6.4) | 10.6 (6.0) | 10.9 (7.1) |
| Δ DB 12 mo | 1.5 (4.3)* | −0.6 (3.5) | -1.2 (4.7) |
| Δ LTSE 18 mo | 1.9 (14.0) | −0.3 (3.9) | -1.3 (4.5) |
| **GGT (U/L)** | | | |
| DB Baseline | 329.4 (506.6) | 267.0 (177.8) | 277.0 (229.3) |
| Δ DB 12 mo | -16.0 (190.6) | -149.4 (157.1)*** | -188.3 (166.8)*** |
| Δ LTSE 18 mo | -176.7 (406.4)** | -161.7 (156.0)*** | -143.3 (157.0)*** |
| **ALT (U/L)** | | | |
| DB Baseline | 55.7 (31.5) | 65.4 (42.5) | 57.0 (43.3) |
| Δ DB 12 mo | -5.3 (19.6) | -23.8 (22.7)*** | -25.0 (28.3)*** |
| Δ LTSE 18 mo | -22.1 (25.0)*** | -25.8 (27.1)*** | -17.5 (57.5)* |
| **AST (U/L)** | | | |
| DB Baseline | 47.3 (18.2) | 54.1 (27.6) | 51.1 (34.4) |
| Δ DB 12 mo | 1.9 (35.0) | -12.9 (15.1)*** | -14.3 (20.5)*** |
| Δ LTSE 18 mo | -10.4 (15.2)*** | -13.1 (17.9)*** | -12.7 (32.4)** |

*$p < 0.05$, **$p < 0.01$, ***$p < 0.0001$. Values are Mean (SD). P-values for the within treatment comparisons are obtained using a paired t-test. All patients represented received ≤ 10 mg OCA.

**Conclusion:** OCA treatment improves liver biochemistry, most notably ALP and GGT, which is sustained throughout the course of the LTSE. Pruritus was the most common AE, but its incidence appeared to lessen with longer treatment.
**Disclosure of Interest:** M. Trauner: Advisory Committees or Review Panels: MSD, Janssen, Gilead, Abbvie; Consulting: Phenex; Grant/Research Support: Intercept, Falk Pharma, Albireo; Patent Held/Filed: Med Uni Graz (norUDCA); Speaking and Teaching: Falk Foundation, Roche, Gilead.
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P. Andreone: Advisory Committees or Review Panels: Janssen-Cilag, Gilead, MSD/Schering-Plough, Abbvie; Speaking and Teaching: Gilead, BMS.
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C. Bowlus: Advisory Committees or Review Panels: Gilead Sciences, Inc; Grant/Research Support: Gilead Sciences, Inc, Intercept Pharmaceuticals, Bristol Meyers Squibb, Takeda, Lumena, Merck; Speaking and Teaching: Gilead Sciences, Inc.
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All other authors have declared no conflicts of interest.

## P0065 EUS FOR SUSPECTED CHOLEDOCHOLITHIASIS. FIRST RESULTS OF A CHANGE IN STRATEGY REGARDING INDICATION AND TIMING OF ERCP

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**Introduction:** Endoscopic ultrasonography (EUS) is a diagnostic modality with excellent diagnostic accuracy for diagnosing common bile duct (CBD) stones. In studies showing these performance characteristics, any EUS with positive findings was instantly followed by an ERCP. In a recent retrospective study, the proportion of positive findings at ERCP in the group of patients with EUS-confirmed bile duct stones was relatively low (58%). This appeared to be related to both the time interval between EUS and ERCP (median 4 days, interquartile range 1–15) allowing for spontaneous stone and sludge passage, as well as the decision to regard biliary sludge as an indication for performing an ERCP. In the current prospective study, we aim to re-evaluate the time interval and the proportion of positive findings on ERCP. Moreover, we adopted a more conservative attitude towards patients with mild symptoms and a non-dilated CBD with sludge at EUS.
**Aims & Methods:** Between January 2015 and March 2016, 40 out of 100 (40%) consecutive patients undergoing EUS for suspected bile duct lithiasis had positive findings. Patients with CBD stones on EUS all underwent an ERCP with endoscopic sphincterotomy. In patients with suspected sludge, a non-dilated CBD on EUS and mild symptoms, we discussed with the patient either to perform an ERCP or to adopt a watchful waiting strategy. Patients with CBD sludge on EUS opting for the conservative strategy were followed regularly at the outpatient clinic. Data were compared to our retrospective series.
**Results:** Thirty-four out of 40 (85%) patients with positive findings during EUS had one or more CBD stones. Six of those only had sludge in the CBD. For the latter indication, ERCP and sphincterotomy was performed in only one patient. In the remaining 5 patients, a watchful waiting strategy was adopted. None these patients developed cholangitis, pancreatitis or developed any indication for ERCP for biliary symptoms at six months follow-up. In patients in whom an ERCP was performed, 26 of 35 (74.3%) had positive findings. This was substantially higher compared to our retrospective series. The time interval between EUS and ERCP was 2 days (interquartile range 1–8) which was significantly shorter compared to our retrospective series (4 days, $p = 0.05$). Sludge was detected and removed in 3 out of 35 cases (8.5%), and one or more stones were found in 23 out of 35 cases (66%). The one patient with CBD sludge at EUS had an unremarkable ERCP. Patient characteristics including age, gender and cholecystectomy history were comparable in both the retrospective and prospective cohorts.
**Conclusion:** Shortening the time interval between EUS and ERCP results in a higher proportion of positive findings at ERCP as expected. Although evidence is still limited, a more conservative approach, i.e. not immediately performing an ERCP in patients with mild non-specific symptoms with sludge in a non-dilated CBD, appears justifiable without an apparent increase in the incidence of biliary complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0066 NEW METHOD TO INSERT LARGE CALIBER PLASTIC AND SELF-EXPANDING METAL STENTS DURING BALLOON OVERTUBE ENTEROSCOPY (BAE) ASSISTED ERCP

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**Introduction:** BAE-assisted techniques have greatly enhanced our ability to perform ERCP in patients with surgically altered upper gastrointestinal (GI) tract anatomy. However, even with newer endoscopes it is impossible to advance self-expanding or larger diameter stents through the working channel, thus impeding successful therapeutic interventions in some patients. We have developed a novel technique (''BAE-ERCP rendezvous and overtube-in-situ'') to place large diameter self-expanding metal stents.
**Aims & Methods:** The aim of this study is to demonstrate a new method to deliver self-expanding metal stents (SEMS) and large diameter stents in patients with surgically altered upper GI tract anatomy. Retrospective, observational, cohort study at a single tertiary, academic institution during a 3-year period evaluating patients with complex post-surgical anatomy and undergoing BAE-ERCP. Description of endoscopic technique: The technique consists of utilizing the overtube as a ''giant working channel'', inserting a wire into the bile ducts, removing the scope, and then inserting the self-expanding stent over the wire, through the overtube under fluoroscopic control. In addition, the overtube may be left in situ to allow for insertion of standard or ultraslim scopes to perform direct cholangioscopy, laser lithotripsy and stone removal. In addition, SEMS can be placed percutaneosuly, under direct endoscopic vision, especially if the scope/overtube are in twisted and angled positions, thus impeding the use of the working channel to advance accessories towards the bile duct.
**Results:** We performed a total of 105 BAE-ERCPs in 90 patients. The BAE-ERCP rendezvous and overtube-in-situ technique was utilized 10 times in 8 patients (8.8%, female n = 4, male n = 4, mean age 54.4, range 22–82). Indications were cholangitis n = 4, choledocolithaisis n = 6, cancer obstructing the hepaticojejunostomy (HJ) n = 2. The post-surgical anatomy was Roux-en-Y HJ n = 5, RY gastric bypass n = 1, Billroth II n = 1. Four patients had undergone a liver transplant, three patients had undergone Whipple's operation for pancreatic cancer, one patient had undergone RY hepaticojejunostomy for a choledocal cyst during childhood. The technique was successful in all patients. In 50% patients other interventions such direct cholangioscopy, dilation and EHL could be performed using this new technique. The mean duration of the procedure was 65 minutes, range 45 to 125 min. There were no major adverse events.
**Conclusion:** The BAE-ERCP rendezvous and overtube-in-situ and rendezvous technique is a useful method to perform therapeutic interventions such as insertion of large caliber stents and self-expanding metal stents in patients with surgically altered upper GI anatomy and in whom traditional BAE-ERCP is impossible. To the best of our knowledge this is the largest experience using this technique. The working channel of DBE and SBE enteroscopes is too small for passage of larger accessories and the deployment of larger diameter stents. The flexibility of the overtube used for enteroscopy an left in-situ allows for smooth passage of the stent delivery system usig radilogical guidance. Knowledge of this level IV ERCP technique is important for those endoscopists performing therapeutic ERCP in patients with surgically altered upper GI tract, as it will likely increase the success rate of BA-ERCP and should thus be added to the therapeutic arsenal of the biliary endoscopist.

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## P0067 TEMPORARY PLACEMENT OF BILIAY PIGTAIL STENTS AFTER UNCERTAIN COMMON BILE DUCT STONES CLEARANCE IN ERCP

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**Introduction:** Sometimes it is difficult to ascertain that after an ERCP session for Common Bile Duct (CBD) stones removal, a complete clearance has been achieved. Failure in total stone extraction can lead to severe cholangitis. There are several methods to verify full CBD stones removal such as occlusion cholangiography, cholangioscopy or intraductal ultrasound. Occlusion cholangiography must be performed carefully for the risk of biliary overdistension and the other methods are not available in many units.
**Aims & Methods:** After ERCP for CBD stones extraction with uncertain complete stone clearance a 7 F, 7 cm long double pigtail stent was inserted. If both patient's condition and liver biochemistry improved, the stent was removed by gastroscopy a month later. After stent removal instructions were given to the patient and relatives for early recognition of cholangitis or CBD obstruction (e.g. dark urine).
**Results:** 24 patients were included prospectively in the study. CBD stone size ranged 9–13 mm. All patients had biliary sphincterotomy and 15 (62.5%) had also sphincteroplasty with balloons up to 15 mm in diameter during the same procedure. Choledocholithiasis tried to be removed with extraction balloons. Doubts about complete CBD stone extraction came about for the following reasons: patient instability and need for a quick procedure (9 or 38%), poor fluoroscopy quality (5 or 21%) and total number of visualized extracted stones less than expected (10 or 41.5%). Two mild pancreatitis and a mild hemorrhage occurred after the procedures. No cholangitis was seen. Uneventful pigtail stent removal was performed a month later and no complications were reported. This group of 24 patients was compared with an historic cohort of 115 previous patients in whom stents were not inserted. Three jaundice episodes and four cholangitis were observed after ERCP for CBD stone extraction in the historic non-stented patients (7/115 or 6%) compared with none in the present group with stents ($p < 0.05$).
**Conclusion:** Insertion of temporary plastic pigtail stents in patients with uncertain complete stone removal in ERCP appears a simple and safe procedure that prevents complications. In this study the stents were removed a month later by gastroscopy without further ERCPs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0068 ASSESSMENT OF SHORT SINGLE-BALLOON ENTEROSCOPE (SHORT-SBE) FOR THERAPEUTIC ERCP IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY

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**Introduction:** Endoscopic retrograde cholangiopancreatography (ERCP) in patients with altered gastrointestinal anatomy is technically challenging. We performed ERCP in such patients using a short single-balloon enteroscope (Short-SBE, Olympus), which has a 3.2-mm working channel and a 152-cm working length and for which conventional accessories are available.
**Aims & Methods:** This study aimed to assess the efficacy and safety of ERCP using a Short-SBE in patients with altered gastrointestinal anatomy. The present retrospective study included 67 patients (range, 37–87 years) and 105 procedures comprising Roux-en-Y reconstruction (55 patients and 73 procedures), Billroth II gastrectomy (7 patients and 16 procedures), and reconstruction by the modified Child method (5 patients and 16 procedures) performed using a Short-SBE. The success and complication rates of each procedure were evaluated.
**Results:** The blind end was reached in 91.4% of procedures (96/105). Of the failed procedures, six were caused by jejunum invasion. Among 96 procedures in which the blind end was reached, cholangiography was successfully performed 93.8% of procedures (90/96). Treatment was successful in 91.7% of procedures (88/96). Successfully performed therapeutic interventions included nasobiliary drainage (n = 2), plastic stent placement (n = 14), self-expandable metallic stent placement (n = 11), tumor biopsy (n = 2), and stone extraction (n = 59) using endoscopic sphincterotomy (n = 1) endoscopic papillary balloon dilation (n = 4), endoscopic papillary large-balloon dilation (n = 19), and choledochojejunostomy dilation (n = 9). Complications that occurred in 10.5% of procedures (11/105) included minor perforation (n = 2) during choledochojejunostomy dilation, mild pancreatitis (n = 5), and mild cholangitis (n = 4). No complications associated with the use of short SBE were observed in the present study.
**Conclusion:** ERCP using a short-SBE is effective and safe in patients with altered gastrointestinal anatomy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0069 ROLE OF SPYGLASS$^{TM}$-CHOLANGIOSCOPY: FIRST CLINICAL EXPERIENCES IN SWITZERLAND

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**Introduction:** Direct cholangioscopy enables not only the direct diagnostic visualisation of the biliary tract, such as the workup of stenosis, but offers also the possibility in treating complicated choledocho- or hepaticolithiasis via cholangioscopic electrohydraulic lithotripsy (EHL). The SpyGlass$^{TM}$ DS cholangioscope (Boston Scientific) is attached to a duodenoscope, inserted into the working channel of the duodenoscope and advanced into the biliary tract as a single operator system. It has got a 10Fr diameter and a working channel of 1.2 mm. The tip of the SpyGlass$^{TM}$ catheter is steerable in 4 directions.
**Aims & Methods:** Prospective inclusions of direct cholangioscopies with SpyGlass$^{TM}$ DS cholagioscope at a tertiary referral centre in Switzerland.
**Results:** Since September 2015, 14 cholangioscopies were performed in 11 patients (3 female, 8 male; mean age 62; ASA I-II; general anaesthesia (3), conscious sedation (11)). Overall, indications were stenosis (6), hepatico-/choledocholithiasis (4), stent dislocation (2), recurring haemobilia (1) and bile leakage (1). The following interventions were performed: electrohydraulic lithotripsy (EHL) with stone removal (2), percutaneous transhepatic cholangiography with cholangioscopy via PTC and EHL of hepaticolithiasis (2) in a patient with hepaticolithiasis after Kasai procedure in childhood for biliary atresia, and stent extraction (1). In diagnostic cholangioscopies, indications were stenosis (6), in one case with known PSC, recurring haemobilia (1), and postoperative bile leakage (1). Visual examination without additional cytology was able to define inflammatory aetiology of stenosis in 5 patients. Additional cytology confirmed this visual diagnosis in 1 case, but was false negative in one case of suspected cholangiocellular carcinoma (CCA) which was confirmed during surgery. In the case of recurring haemobilia with several unsuccessful prior ERCs, diagnosis of a CCA was made by direct cholangioscopy.
**Conclusion:** First experiences with SpyGlass$^{TM}$ -Cholangioscopy in clinical practice show a therapeutic as well as a diagnostic benefit due to its high resolution imaging. Its simple application (single operator system) is a relevant factor in clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0070 BALLOON-OVERTUBE ENTEROSCOPY ASSISTED (BAE) VERSUS LAPAROSCOPY-ASSISTED ERCP IN BARIATRIC POST-ROUX-EN-Y GASTRIC BYPASS PATIENTS: A COMPARATIVE STUDY

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**Introduction:** Data on balloon enteroscopy–assisted ERCP (BAE-ERCP) versus laparoscopy-assisted ERCP in post–Roux-en-Y gastric bypass (RYGB) patients are scarce.
**Aims & Methods:** The aim of this study was to compare BEA-ERCP with laparoscopy-assisted ERCP post-RYGB patients. This is a retrospective, observational, comparative, non-randomized, cohort study of consecutive patients at a single tertiary, academic institution during a 3-year period evaluating patients with Roux-en-Y gastric bypass undergoing BAE-ERCP or laparoscopy-assisted ERCP.
**Results:** A total of 31 patients underwent 35 procedures (29 female, 2 male, mean age 52.4 years, range 32 to 67). A total of 19 patients underwent laparoscopy-assisted ERCP and 12 patients underwent BAE-ERCP. There were no statistically significant differences in age (51.5 vs. 52.1 years), gender (9 vs. 5%), indication for ERCP (choledocolithiasis in 73 vs. 67%, suspected sphincter of Oddi dysfunction, 26 vs. 27%). Laparoscopy-assisted ERCP was superior to BAE-ERCP in papilla identification (100% vrs 67%, $p < 0.01$). The ERCP success rate was also higher in the laparoscopy-assisted ERCP group as compared to the BAE-ERCP group (89% vs. 50%, $p < 0.01$). Deep cannulation of the common bile duct failed in one patient undergoing laparoscopy-assisted ERCP, in another patient it was impossible to remove the large impacted stones within the CBD. In three patients undergoing BAE-ERCP it was impossible to perform therapeutic biliopancreatic interventions despite successfully entering the biliodigestive limb. Although the procedure duration was much longer during laparoscopy-assisted ERCP (the mean total time including operation was 190 minutes), the total ERCP time was similar (laparoscopy-assisted ERCP 63 minutes, range 22 to 110 min. vs. BAE-ERCP with a mean of 65 min, range 45 to 125 min). The hospital duration was 2.3 days in the laparoscopy-assisted ERCP group and 1.2 day in the BAE-ERCP group ($p = 0.02$). There were no major complications in the BAE-ERCP group. In patients undergoing laparoscopy-assisted ERCP there were two post-ERCP pancreatitis and one severe post-sphincterotomy bleeding requiring blood transfusion and surgical re-intervention.
**Conclusion:** LA-ERCP offers a higher chance of therapeutic success in patients with Roux-en-Y gastric bypass. Nevertheless, as BAE-ERCP also leads to therapeutic success in about 50% of cases, and thus, starting with BAE-ERCP may offer a stepwise approach and avoid more invasive procedure, longer hospitalization and possibly be more cost-effective than LA-ERCP.
**Disclosure of Interest:** K. Mönkemüller: Honoraria for speaking/lectures/education - Cook Medical, USA; Ovesco, Tuebingen, Germany.
All other authors have declared no conflicts of interest.

## P0071 IS THE PERIAMPULLARY DIVERTICULUM A RISK FACTOR FOR POST ERCP PANCREATITIS ACCORDING TO TYPE AND SIZE?

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**Introduction:** We investigated whether periampullary diverticulum (PAD) would be different effects aspect of post endoscopic retrograde cholangiopancreatography (ERCP) pancreatits (PEP) according to type and size of PAD. The aim of this study was to investigate risk factors for PEP, including three types of PAD.
**Aims & Methods:** Consecutive ERCP procedures for extractions of common bile duct stones were studied at one university hospital in Chucheon, Korea from Jan 2007 to July 2015. We reviewed the medical charts of 959 patients, PAD were classified into three types by the location of ampulla of Vater: type 1, inside the diverticulum; type 2, on the margin of diverticulum; type 3, outside the diverticulum. PAD size was divided to Group 1 (larger than diameter of ampulla of Vater (AoV)), Group 2 (similar with diameter of AoV) and Group 3 (smaller than AoV).
**Results:** One hundred sixty-two patients had PAD including 6 (3.7%) in type 1, 107 (66.0%) in type 2, and 49 (30.2%) in type 3. PEP was developed in 61 patients, the frequency of PEP was different from diverticulum type (3.3% in type 1; 82.0% in type 2; 14.8% in type 3, $p = 0.003$). The size of diverticulum was not different for PEP (31.1% in Group1, 47.5% in Group2, 21.3% in Group3, $p = 0.161$). By univariate nanalysis, CBD size (OR 0.898, 95% CI 0.85 – 0.94, $p = 0.0001$) and cannulation time (OR 1.028, 95% CI 1.010–1.046, $p = 0.002$), diverticulum type 2 (OR 2.899, 95% CI 1.72 – 8.8, $p = 0.001$) was associated with PEP. By multivariate analysis, the risk factors for PEP were diviericulum type2 (OR 4.34, 95% CI 1.49 – 12.55, $p = 0.007$).
**Conclusion:** Periampullary ampullary diverticulum, type 2 is only independent risk factor for PEP in our study.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0072 INTRADUCTAL PLASTIC STENT PLACEMENT IS AN EFFECTIVE THERAPY FOR MALIGNANT BILIARY STRICTURES

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**Introduction:** Recent reports have described the efficacy of plastic stent (PS) placement inside the bile duct for malignant biliary strictures. However, the superiority of intraductal PS placement (IS) over PS placement across the sphincter (conventional PS placement [CS]) and uncovered metallic stent placement above the sphincter of Oddi (MS) is unclear.
**Aims & Methods:** The aim of this study was to evaluate the efficacy of IS, and compare its efficacy with the efficacies of CS and MS for malignant biliary strictures. This retrospective study included 25 patients (28 procedures) with an unresectable malignant hilar or middle bile duct obstruction, who underwent IS between January 2008 and December 2015 at our institution. The indication for IS was a distance of at least 3 cm between the lower end of the stricture and the sphincter. We compared the efficacy of IS with the efficacies of CS (22 patients [32 procedures]) and MS (12 patients [12 procedures]). Among the 25 patients who underwent IS, the origins of the malignant biliary stricture were gallbladder cancers in 9 patients, intrahepatic cholangiocarcinomas in 7 patients, bile duct cancers in 3 patients, pancreatic cancers in 3 patients, and others in 3 patiets. We evaluated complications associated with stent placement, stent patency (functional) periods, and stent removability at occlusion. We modified a 7-Fr Flexima biliary stent (Boston Scientific Co., Boston, MA) and attached a nylon thread (size 2/0) to the distal end for removal. If insertion was difficult due to winding or narrowing of the intrahepatic bile duct (ex. B3 and B6), we placed a Flexima nasobiliary drainage tube (7.5Fr), cut to the appropriate length, as an internal stent. All stent placements were performed after preoperative nasobiliary drainage.
**Results:** The overall technical success rates in the IS, CS, and MS groups were all 100%. The success rates for reducing or maintaining the serum bilirubin level (total bilirubin $< 2.0$ mg/dL) were as follows: IS, 96.4% (27/28); CS, 100%; MS, 100%. The median patency duration was greater in the IS group than in the CS group (138 days vs. 44 days, $P < 0.001$, log-rank test); however, the patency duration was not significantly different between the IS and MS groups (138 days vs. 231 days, $P = 0.46$). In the IS group, there were no early complications associated with stent placement; however, delayed complications were observed in 3 patients from this group (2 had cholecystitis with gallstones and 1 had stent migration to the hepatic side). Additionally, in the IS group, 11 patients developed stent occlusion (dysfunction). The causes of occlusion were sludge deposition in 6 patients, reflux cholangitis in 1 patient, bending of the stent in 1 patient, tumor overgrowth in 1 patient, dislocation to the duodenal side in 1 patient, and migration to the hepatic side in 1 patient. In 9 patients from the IS group, stent replacement was attempted and was performed successfully. There were no complications associated with stent removal. Besides IS, the factors associated with PS patency period were the number of stents and usage of anticancer agents (multiple stents 100 days vs. single stent 44 days, $P = 0.034$, usage of anticancer agents 78 days vs. no usage 61 days, $P = 0.024$, log-rank test). Furthermore, multivariate analysis showed a significant difference in IS ($P < 0.0001$, Cox proportional hazard model).
**Conclusion:** The patency period is longer with IS than with CS for malignant biliary obstruction. Additionally, the patency period tends to be shorter with IS than with MS; however, the difference might not be significant. Additionally, complications are relatively minor with IS, and the stent can be removed if dysfunction occurs. Therefore, IS is an effective option for malignant hilar and middle bile duct obstructions, and it is as effective as MS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0073 HUMAN EQUILIBRATIVE TRANSPORTER 1 (HENT1) EXPRESSION IS NOT PREDICTIVE FOR GEMCITABINE OUTCOME IN PATIENTS WITH ADVANCED BILIARY TRACT CANCER

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**Introduction:** Human equilibrative nucleoside transporter 1 (hENT1) is the major transporter responsible for gemcitabine uptake into cells. hENT1 expression has been proposed as one of predictive biomarkers for gemcitabine sensitivity in patients with pancreatic cancer. However, the prognostic roles of hENT1 expression in patients with advanced biliary tract cancer (BTC) have not been evaluated so far. The aim of this study was to investigate the association between the expression of hENT1 and disease outcome in patients with advanced BTC treated with gemcitabine.
**Aims & Methods:** Pathological specimens were collected from 101 BTC patients who received first-line palliative chemotherapy with gemcitabine at Seoul National University Hospital between 2006 and 2013. Immunostainings with Rabbit Anti-Human hENT1 monoclonal antibody (Clone SP120) were performed in those specimens. Interpretations were classified as negative, mild, and moderate, according to the immunostain intensity. The patients were divided into two groups according to hENT1 expression, and compared in terms of overall survival (OS), progression-free survival (PFS), and response rate (RR).
**Results:** Immunostainings of specimens from 101 patients (60 males; mean age, $61.6 \pm 9.2$ years) were interpreted by a single pathologist independently. Twenty-one (20.8%) gallbladder cancers, 18 (17.8%) extrahepatic, and 62 (61.4%) intrahepatic cholangiocarcinomas were included. They consisted of 27 (26.7%) locally advanced and 74 (73.3%) metastatic cancers. Positive hENT1 expression was observed in 49 (48.5%) patients, who showed median $8.77 \pm 1.15$ months of OS and $3.80 \pm 0.68$ months of PFS, with no significant difference compared with the negative group. RR of positive group (49.0%) was also not significantly different from that of negative group (48.1%). When negative and mild intensity were classified as low expression, OS, PFS, and RR were also not significantly different between low and high expression group.
**Conclusion:** There was no evidence supporting the use of hENT1 as a predictive marker for gemcitabine efficacy in patients with advanced BTC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0074 ROLE OF THE NEW GENERATION SINGLE-OPERATOR CHOLANGIOSCOPY IN THE DIAGNOSIS OF INDETEREMINATE BILIARY LESIONS: A SINGLE TERTIARY CENTRE PROSPECTIVE STUDY

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**Introduction:** Recent improvements in cholangioscopy include a 4-fold increase in visual acurity for the Spyglass DS cholangioscope compared with previous version. The accuracy of cholangioscopy views and guided sampling (SpyBite) using the new generation Spyglass has yet to be evaluated.
**Aims & Methods:** Prospective single-arm, single-centre study collected data from all patients referred to our tertiary centre to undergo ERCP with cholangioscopy between June 2015 and March 2016. All patients were discussed in the pancreatobiliary multidisciplinary meeting before and after the procedure. The aim of this study is to compare the diagnostic accuracy between brush, endobiliary biopsies, SpyBite and cholangioscopic impression by the endoscopist (likely benign/malignant).

**Results:** A total of 92 patients underwent cholangioscopy; n = 25 (27%) for indeterminate strictures, n = 66 (72%) for stones, n = 2 other. The mean age of the group with strictures (12 males) was 56 +/- 16 years. Stricture location: distal CBD n = 8 (36%), mid CBD n = 3 (14%), CHD n = 2 (9%), hilum n = 6 (27%), intrahepatic n = 2 (9%) or extensive cholangiopathy n = 1 (5%). Two patients had normal mucosa and no biopsies were taken. One patient had a PD stricture. 12 patients had a relevant past medical history: PSC n = 5, IgG4 n = 1, possible metastatic cancer n = 3, other auto-immune disease n = 2 and previous biliary surgery n = 1. Results showed brush cytology sensitivity 53%, specificity 100%, positive predicitive value (PPV) 100%, negative predictive value (NPV) 25%; SpyBite sensitivity 67%, specificity 100%, PPV 100% and NPV 58%; cholangioscopic views 100% sensitivity, 73% specificity, PPV 77% and NPV 100%. One patient developed mild post-ERCP pancreatitis and one patient had abdominal pain following endoscopy without proven pancreatitis or perforation.
**Conclusion:** The new generation cholangioscope has shown a significant improvement in diagnostic yield which appears to relate to improved visualisation in addition to histological confirmation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0075 DEVELOPMENT OF AN EXTERNAL-TO-INTERNAL CONVERTIBLE ENDOSCOPIC BILIARY DRAINAGE DEVICE

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**Introduction:** Endoscopic nasobiliary drainage (ENBD) for a malignant biliary stricture has some advantages over endoscopic retrograde biliary drainage (ERBD) which is the internal drainage. ENBD, allowing external drainage, enables not only drainage but also cytological and bacteriological examination. It also contributes to diagnosis by enabling detailed cholangiography after drainage. However, ENBD may cause stress due to naso-pharyngeal discomfort. ERBD obviates this stress, but it makes the above-mentioned examinations almost impossible. Therefore, we have developed an external-to-internal convertible endoscopic biliary drainage (ETI-EBD) device that enables both, internal and external drainage with a single endoscopy. Herein, we report the method and the feasibility of this device.
**Aims & Methods:** The ETI-EBD device consists of 3 parts, comprising a 5-Fr ENBD tube (250 cm) (ENBD-t), an 8.5-Fr ERBD tube (7 cm) (ERBD-t), and an 8-Fr pusher tube for ERBD (230 cm) (P-t). The ERBD-t and the P-t are mounted over the ENBD-t. The ERBD-t is positioned 12 cm from the distal end of the ENBD-t. The P-t is placed between the proximal end of ERBD-t and about 10 cm of the proximal end of the ENBD-t. The proximal end of P-t is firmly fastened to the ENBD-t. Insertion of the ETI-EBD device was similar to that of the conventional ENBD-t. After passing the guidewire through the stricture in the bile duct under ERCP, the device was inserted over the guidewire through the endoscopic channel. When the proximal end of the ERBD-t was inserted to the papilla, the duodenal endoscope was withdrawn, leaving the device in place. Then, the device was exchanged from the mouth to the transnasal route. At this time, both, ERBD-t and P-t remained secured over the ENBD-t. After ENBD and bile collection, external-to-internal conversion was performed as follows: the fixation between ENBD-t and P-t was released and only the ENBD-t was withdrawn from the P-t. P-t was gripped so as not to be withdrawn with the ENBD-t. Then, ERBD-t was isolated from P-t and ENBD-t. Finally, we were able to leave only the ERBD-t between the duodenum and the bile duct without endoscopy or radiography.
**Study design:** We evaluated the ETI-EBD device in a preliminary, prospective feasibility study. We enrolled 18 consecutive patients with a malignant biliary stricture between January 2015 and December 2015.
**Results:** A total of 14 patients were evaluated in the present study, because we had to exclude 4 patients who failed to be passed a guide wire through the stricture. ETI-EBD was successfully completed in all 14 patients (100%). The median time of placing of this device was 20 hours (1–47 hours). The median time of placing the ERBD-t after removal of ENBD-t was 27 days (7–83 days). The reasons for discontinuation of ERBD were ERBD-t obstruction in 3 patients, conversion to a metallic stent in 6 patients, surgery for the stricture in 2 patients, and death in 3 patients. There were no significant complications associated with the use of the device.
**Conclusion:** We have introduced a new device that has shown favorable feasibility and has enabled both, external and internal biliary drainage with a single endoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0076 A PROGNOSTIC MODEL ADOPTING NEW CRITERIA OF INVASION DEPTH IN DISTAL BILE DUCT CANCER: A BETTER PREDICTOR OF SURVIVAL THAN PREVIOUS METHODS

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**Introduction**: The 7th AJCC staging system is well known to effectively predict the prognosis of DBD cancers. However, published data showed that AJCC staging system is not reliable to predict patient's survival in DBD cancer. The unexpected results could be related to inter-observer variation induced by confusion among pathologists in microscopic evaluation according to ambiguous description of AJCC staging system.
**Aims & Methods:** Depth of invasion (DOI) is an important prognostic factor for patients with distal bile duct (DBD) carcinoma. This study aims to identify the optimal cut-off value of DOI in relation to the prognosis in patients with DBD cancer. Data of 179 patients with DBD adenocarcinoma treated in 3 institutions in Korea were investigated. At microscopic review, DOI was measured. The relationships between clinicopathological parameters and groups based on depth of invasion ($\leq$3 mm; 3–10 mm; $>$10 mm) were evaluated, and the survival time of each group based on DOI and 7$^{th}$ AJCC T classification was compared.
**Results:** The deeply invading tumor exhibits more tendency towards infiltrative type, high histological grade, AJCC stage, and nodal metastasis, pancreatic, duodenal, lymphovascular and perineural invasions. The measured DOI was significantly correlated with worse disease-free and overall survival (all. $p < 0.05$). In multivariate analyses, after adjusting confounders, grouping based on invasion depth remained as one of the prognostic factors (all, $p < 0.05$), while that of T classification was not significant.
**Conclusion:** On basis of proposed cut-off value, the DOI could be clear and meaningful concept overcoming the vagueness of the T classification in predicting clinical outcomes in patients with DBD carcinoma. Invasion depth should be measured on histopathological assessment of DBD carcinomas.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0077 A PROSPECTIVE STUDY TO ASSESS THE SAFETY AND EFFICACY OF USING AIR FOR CHOLANGIOGRAPHY IN PATIENTS WITH HILAR STRICTURES, HIGH CHOLANGIO CARCINOMA IN CHD AND CHD STRICTURES SECONDARY TO CARCINOMA GALL BLADDER

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**Introduction:** To assess the safety and efficacy of using air for cholangiography in patients with hilar strictures, high cholangio carcinoma in CHD and CHD strictures secondary to carcinoma gall bladder.
**Aims & Methods:** A prospective study to assess the safety and efficacy of using air for cholangiography in patients with hilar strictures, high cholangio carcinoma in CHD and CHD strictures secondary to carcinoma gall bladder. 90 patients, from 1$^{st}$ October 2010 to 31$^{st}$ October 2015, who came with obstructive jaundice for stenting with strictures at high CHD or hilum (Type 1 and Type II Strictures only) due to cholangiocarcinoma and carcinoma gall bladder were included in this study. 10 cc of air was injected slowly and the ductal anatomy outlined. Ease of identification of various segments of liver, length of stricture, proximal limit of the stricture, possibility of placing stents, risk of cholangitis and complications was studied.

**Results:** Total cases – 90. Etiology: Carcinoma GB – 59 (65.5%), Hilar Type 1 -21 (23.3%), Hilar Type II – 10 (9%). Successful normal cannulation at ERCP – 61 (67.8%), Precut Used – 29 (32.2.%). Ductal anatomy outlined – 90 (100%). Proximal end of stricture identified – 90 (100%). Classification of stricture possible – 87 (96.7%) – 3 cases had Type III and III B strictures which were not clearly outlined. Dilatation and stenting possible: 85 (94.4%), Single stent – 40 (44.4%), Double stenting -50 (44.4%). Complications: Air embolism – 0 (0%), Cholangitis – 2 (2.22%) – Non affording patients, plastic 10 Fr stents were placed. Days of hospitalization – 2.5 (1 to 5).
**Conclusion:** 1. Air cholangiography is a feasible and safe option in high CHD and Hilar bile duct malignant strictures. 2. High success of identifying ductal anatomy and successful placement of stents in the desired segment is possible. 3. Complications are very rare and no case of air embolism was noted in our study.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0078 USEFULNESS OF SHORT-TYPE BALLOON-ASSISTED ENDOSCOPES AND METALLIC STENTS WITH A SMALL-DIAMETER DELIVERY SYSTEM FOR MALIGNANT BILIARY OBSTRUCTION WITH SURGICALLY ALTERED ANATOMY

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**Introduction:** With the advent of the short-type balloon-assisted endoscopes, endoscopic biliary drainage for malignant biliary obstruction (MBO) is possible in surgically altered anatomy. Moreover, self-expandable metallic stents (SEMS) with a small-diameter delivery system showed longer patency and lower incidence of stent occlusion than plastic stents, which leads to QOL improvement.
**Aims & Methods:** This study was designed to evaluate the usefulness of endoscopic metallic stenting using short-type balloon-assisted endoscopes for MBO with surgically altered anatomy. Between January 2012 and February 2016, short-type double-balloon or single-balloon endoscope-assisted ERCP for MBO was performed in 16 patients with surgically altered anatomy. SEMS with a small-diameter delivery system (5.7Fr–7.2Fr) were used. Technical success rate, clinical success rate, adverse events, and long-term outcomes were evaluated in this retrospective study. Recurrent biliary obstruction (RBO) was defined as a composite of either occlusion or migration, and time to recurrent biliary obstruction (TRBO) refers to the time from SEMS placement to the recurrence of biliary obstruction. TRBO was estimated using the Kaplan-Meier method.
**Results:** A total of 16 patients (12 male, a mean age of 68 years) were enrolled. The causes of MBO included recurrent gastric cancer after total gastrectomy with Roux-en-Y reconstruction (n = 4), recurrent perihilar cholangiocarcinoma after extended hepatic lobectomy (n = 4), recurrent distal cholangiocarcinoma after pancreaticoduodenectomy (PD) (n = 4), recurrent pancreatic cancer after PD (n = 2), recurrent diffuse cholangiocarcinoma after extended hepatic lobectomy and PD (n = 1), and lymph node metastasis of intrahepatic cholangiocarcinoma after distal gastrectomy with Roux-en-Y reconstruction (n = 1).
Technical success rate and clinical success rate were 94% and 88%, respectively. Multiple SEMS were placed using the partial-stent-in-stent method in 4 patients and side-by-side method in 1 patient. Early adverse events (< 30 days) occurred in 2 patients (13%); mild pancreatitis in 2. The median follow-up period was 165 days, the median TRBO was 272 days, and median overall survival was 255 days. The causes of RBO were biliary sludge (n = 4), tumor ingrowth (n = 2), tumor overgrowth (n = 1), and kinking (n = 1). All 8 patients required re-intervention: additional stent-in stent placement of covered SEMS in 2 patients, PTBD in 1 patient, plastic stent in 3 patients, and balloon cleaning alone in 2 patients. Internal biliary drainage could be maintained in 12 patients (75%) until death or the end of follow-up.
**Conclusion:** Endoscopic metallic stenting using short-type balloon-assisted endoscopes for MBO with surgically altered anatomy is technically feasible, safe, and effective, and can contribute to the QOL improvement.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0079 THE SEQUENCE OF BRUSH CYTOLOGY AND INTRADUCTAL BIOPSY DO NOT AFFECT THE DIAGNOSTIC YIELD IN PATIENT WITH BILIARY STRICTURE

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**Introduction:** Confirming malignancy through cytological or tissue diagnosis is essential in patient with biliary stricture, especially considering surgical management. Brush cytology and intraductal biopsy are routinely done during endoscopic retrograde cholangiopancreatography (ERCP) to diagnose malignant biliary stricture. However, whether the sequence of two diagnostic methods affect the diagnostic yield or not is not known well.
**Aims & Methods:** This study was aimed to investigate the diagnostic efficacy according to the sequence of brush cytology and intraductal biopsy in patient with biliary stricture. From January 2010 to December 2015, a total of 364 patients who underwent brush cytology and intraductal biopsy during ERCP for suspicious malignant biliary stricture were reviwed retrospectively at Chonbuk National University Hospital. ERCP was performed by two experienced endoscopists who carried out brush cytology and intraductal biopsy in different sequence according to personal preference. The final diagnosis was confirmed by histocytologic findings or, operation or, clinical and radiologic follow-up at least 6 months.
**Results:** 154 patients underwent brush cytology first and then intraductal biopsy was done, while 210 patient underwent intraductal biopsy first and then brush cytology during ERCP. There was no significant difference in rates of diagnostic accuracy according to the sequence of brush cytology and intraductal biopsy [cytology-biopsy vs biopsy-cytology: 117/154 (76.0%) vs 156/210 (74.3%), p = 0.713]. Overall sensitivity and accuracy of brush cytology was similar with intraductal biopsy [58.8%, 63.7% vs 58.5%, 64.5%]. A combination of both diagnostic methods could increase the sensitivity and accuracy as 72.0% and 75.0%.
**Conclusion:** The sequence of brush cytology and intraductal biopsy did not affect the diagnostic yield in patient with biliary stricture in this study. A combination of both diagnostic methods could increase sensitivity and accuracy. These results suggest that endoscopist can feel free from the sequence of brush cytology and intraductal biopsy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0080 COMPARING LIQUID-BASED CYTOLOGY (CELLPREP®) METHODS WITH CONVENTIONAL SMEAR METHODS FOR ERCP GUIDED BRUSHING CYTOLOGY OF BILE DUCT

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**Introduction:** ERCP-guided brushing cytology has been used worldwide to diagnose bile duct cancer. Bile duct brushings have been recognized as a technique of moderate sensitivity and high specificity in identifying carcinoma of the biliary regions. In the 1990s, Liquid-based cytology (LBC) was developed as an alternative to conventional smear (CS). Recent studies suggests the Liquid-based cytology (ThinPrep) method can improve diagnostic sensitivity and accuracy than conventional smear methods in bile duct brushings. However, there is no a study comparing Cellprep® methods with CS in bile duct cancer.
**Aims & Methods:** The aim of this study was to compare the morphologic features and diagnostic efficacy of LBC with those of CS for ERCP brushing cytology. This is the prospective study. This study was done with total 32 pts who were suspected bile duct cancer. Bile duct diagnosis was used by ERCP guided brushing cytology. Brushing cytology was done more than two. The final diagnosis is done by biopsy, cellblock, and clinical follow up.
**Results:** There were performed 34 brushing cytology in our institution from 32 patients (among them, two patients, it was performed twice). The cytologic diagnoses for both CP and CS were categorized into five main groups: ① inadequate, ② negative, ③ atypical, ④ suspicious for malignancy, and ⑤ malignant. 1 case (2.9%) of CS preparations was inadequate, but 4 cases (11.8%) CP preparations were inadequate. In CP and CS, the negative: 20.6% and 11.8%, atypical cell: 11.8% and 14.7%, suspicious: 5.9% and 11.8%, and malignant: 50% and 55.8%. accuracy: 58.8% and 73.5%. The sensitivity was 57.6% for CP and 72.7% for CS. The specificity and positive predictive value was 100% for both methods.
**Conclusion:** Cellprep® methods (Liquid-based cytology) revealed lower sensitivity and accuracy than conventional smear methods. Thus, cellprep® (liquid-based cytology) methods can not be replaced by conventional smear methods.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0081 PERCUTANEOUS CHOLECYSTOSTOMY AS DEFINITE TREATMENT FOR ACUTE CHOLECYSTITIS WITH UNRESECTABLE KLASTKIN TUMOR

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**Introduction:** Percutaneous cholecystostomy is an effective and safe treatment for acute cholecystitis in critically ill patients. However, it not has been established as definite management of cholecysitis instead of interval cholecystectomyespecially in patients with unresectable klatskin tumor.
**Aims & Methods:** From June 2009 to July 2015, we retrospectively reviewed 47 klatskin tumor patients who received percutaneouscholecystostomy diagnosed as acute cholecystitis. Long-term outcomes following percutaneous cholecystostomywere evaluated. In this study, we evaluated efficacy and safety of percutaneous cholecystostomy as definite management for acute cholecystitis in patients with unresectable klatskin tumor.
**Results:** 47 patients with a mean age of 74 years were identified. The technical and clinical success rates for percutaneouscholecystostomy were 100%. All patients did not receive an interval cholecystectomy. The mean maintenance period of cholecystostomy tube was about 11.5 weeks (range, 3 – 43). 2 patients (4.2%) suffered tube-related complications, including catheter displacement, bile leakage with site infection. 23 patients (48.9%) could removed the cholecystostomy tubes during the follow up period. Seven out of 23 patients (30.4%) suffered recurrent cholecystitis during the follow-up period. The mean time to re-intervention was 8.5 weeks (range, 4–20). They were treated successfully with repeated percutaneous cholecystostomy.
**Conclusion:** Although some patients had recurrent attacks, percutaneous cholecystostomy can be performed as definite treatment for the management of acute cholecystitis. It seems to be a feasible and considerable option in some patients with unresectable klatskin tumor.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 10:30-17:00
**PANCREAS I - POSTER EXHIBITION**

## P0082 THE POSSIBLE GENETIC BACKGROUND OF ALCOHOL-INDUCED PANCREATIC STEATOSIS

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**Introduction:** Alcohol-induced pancreatic disease has got much attention all over the world. Accumulating animal studies and our previous clinical research showed that long-term alcohol administration led to pancreatic steatosis. But its possible genetic background is still unclear. Alcohol-induced pancreatic steatosis is associated with alcohol metabolism in the pancreas, in which alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are the major oxidative enzyme. And genetic polymorphism of ADH2 and ALDH2 is known to be closely related to alcohol dependence. But it is still unknown whether genetic polymorphism of them is also relevant to pancreatic steatosis in alcoholics.
**Aims & Methods:** This study aims to find out the possible genetic background of alcohol-induced pancreatic steatosis in alcoholics by analyzing genetic polymorphism in ADH2 and ALDH2. 163 alcoholic male aged 20 ~ 70 years with a normal body mass index were recruited into this study. The alcoholics were defined as the drinkers with an alcohol intake of >80 g/day, a duration of >5 years, and abstinence from alcohol within 2 years. They received magnetic resonance scanning in the epigastric region by using double-echo chemical shift magnetic resonance technique. PCR- restriction fragment length polymorphism was used for ADH2 and ALDH2 genotype detection. The drinkers with pancreatic fat content higher than ≥4.2%, ≥8.0% in alcoholics younger and older than 50 years respectively were diagnosed as alcohol-induced pancreatic steatosis. This study was approved by the Chinese Clinical Trial Registry Clinical Trial Ethics Committee (registration number:ChiCTR-CCH-00000147) and the Ethics Committee of West China Hospital of Sichuan University. And it conform to the principles of the Declaration of Helsinki of the World Medical Association. Informed consent was obtained from each participant before enrollment.
**Results:** The distribution of the different ADH2 and ALDH2 genotypes among the 163 alocholics closely conformed to expected Hardy-Weinberg frequencies ($p > 0.05$). In drinkers, compared with ADH2*2/*2 carriers, ADH2*1/*1 carriers showed a significantly elevated risk of developing pancreatic steatosis (<50 years, OR = 6.73; >50 years, OR = 5.34). No association was found between ALDH2 genotypes and risk of pancreatic steatosis.
**Conclusion:** In drinkers, ADH2*1/*1 carriers had a significantly higher risk to develop alcohol-induced pancreatic steatosis. ADH2*1/*1 genotype may be related to alcohol-induced pancreatic steatosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0083 BETAINE ATTENUATES ALCOHOLIC FATTY PANCREAS THROUGH DOWN-REGULATION OF DGAT2

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**Introduction:** Our previous studies have shown that betaine could attenuate alcoholic fatty pancreas by down-regulation of sterol regulatory element binding protein-1 c. However, whether diacylglycerol acyltransferase (DGAT) 1/2 and peroxisome proliferator-activated receptor λ coactivator (PGC)-1α, which also play important roles in alcohol-induced disorders of lipid metabolism, are involved in the antisteatotic effects of betaine remains to be explored.
**Aims & Methods:** This study aims to explore the effect of betaine on pancreatic DGAT1/2 and PGC-1α in rats with alcoholic fatty pancreas and its possible mechanism. 36 Wistar rats were randomly divided into control, ethanol and ethanol + betaine groups and given the following as their only water source respectively: water, ethanol containing water (25%, vol/vol), or ethanol containing water (25%, vol/vol) plus betaine (1%, wt/vol) for six months. Morphological changes of the pancreas were observed by hematoxylin-eosin staining, oil red O staining and transmission electron microscope. Pancreatic triglyceride (TG) and free fatty acid (FFA) levels were assessed by enzymatic colorimetric methods. Adiponectin levels in the pancreas and serum were measured by enzyme-linked immunosorbent assay. Pancreatic adiponectin receptor (AdipoR) 1/2 protein expression were detected by immunohistochemistry and Western blot. Pancreatic mRNA expression of AdipR1/2, DGAT1/2 and PGC-1α were determined by quantitative reverse transcriptase PCR (qRT-PCR). DGAT2 expression in SW1990 pancreatic adenocarcinoma cells treated with ethanol (100 mmol/L) or ethanol (100 mmol/L) plus betaine (168 mmol/L) and/or adiponectin (0.5 μg/mL) was determined by qRT-PCR.
**Results:** Betaine significantly alleviated the alcohol-induced accumulation of lipid droplets in the pancreatic acinar cells. Pancreatic TG and FFA levels were greatly elevated by 91.2% and 92.3% in ethanol group when compared with controls ($p < 0.05$). And pancreatic TG and FFA contents were markedly reduced by 40.8% ($p < 0.05$) and 61.5% ($p < 0.01$) in ethanol + betaine group when compared with those in ethanol group and were maintained at control levels. The adiponectin levels in the pancreas and serum of ethanol-fed rats were dramatically reduced by 45.4% and 62.5% when compared with the controls ($p < 0.01$). And adiponectin levels in the pancreas and serum were elevated by 110.6% and 98.3% in ethanol + betaine group compared with those in ethanol group ($p < 0.05$) and were sustained at control levels. Compared with control group, ethanol group showed significantly down-regulated protein level of AdipoR1 and mRNA expression of AdipoR1 and PGC-1α in the pancreas ($p < 0.05$). And pancreatic AdipoR1 mRNA and protein levels were greatly enhanced in ethanol + betaine group compared with those in ethanol group ($p < 0.01$) and were similar to controls. However, pancreatic PGC-1α mRNA expression in ethanol + betaine group was still lower than that of control group ($p < 0.01$) and were similar to that of ethanol group. Moreover, pancreatic DGAT2 mRNA level was significantly elevated by ethanol consumption ($p < 0.01$) and was markedly down-regulated to control levels with the addition of betaine. However, no significant difference was observed in the expression of DGAT1 and AdipoR2 in the pancreas between the three groups. In vitro, betaine or/and adiponectin significantly suppressed alcohol-induced up-expression of DGAT2 mRNA ($p < 0.01$), whereas no difference was observed between the effects of the sole betaine, sole adiponectin and the combination of betaine and adiponectin.
**Conclusion:** Betaine attenuated alcoholic fatty pancreas probably by suppressing alcohol-induced DGAT2 up-regulation in the pancreas through both the restoration of pancreatic adiponectin signaling and the direct effect of betaine on acinar cells.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0084 EXPRESSION OF INSULIN AND GLUCAGON IN LIVER AND PANCREAS IN RAT COPPER-DEFICIENT MODEL OF INJURY

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**Introduction:** The copper-deficient model of injury is one for studying pancreas regeneration, where we can see destruction of pancreatic parenchyma, concomitant liver injury and regeneration of both organs during the recovery phase of the experiment.

**Aims & Methods:** The aim of our work was to study the expression of insulin and glucagon in pancreas and liver tissue in rat copper-deficient model of injury. 24 white Wistar male rats (80–100 g weight) were maintained on copper-deficient diet (MP Biomedicals, USA) containing a relatively non-toxic copper-chelating agent, triethylenetetramine tetrahydrochloride in final concentration of 0.6% w/w for 8 weeks, and then returned to normal rat chow for another 8 weeks (recovery phase). Groups of 3 animals each were killed after 2, 4, 6, and 8 weeks of copper-deficient diet and 2, 4, 6, and 8 weeks of recovery phase. Paraffin sections of liver and pancreas were stained immunohistochemically using antibodies to insulin and glucagon. The level of these hormones was measured in venous blood of rats.

**Results:** After 4 weeks of copper-deficient diet we observed glucagon-positive cells in peripheral part of the islets as well as single glucagon-positive cells and their clusters resembling newly formed islets. Expression of glucagon was maximal after 8 weeks of diet and continued to be at the same level 2 and 4 weeks after rats were returned to normal rat chow. Groups of glucagon-positive hepatocyte-like cells were found in the pericentral areas of liver, solitary glucagon-positive hepatocyte-like cells in liver parenchyma during all weeks of our experiment. The maximum of glucagon expression in liver was detected 2 weeks after return to normal rat chow. Glucagon-positive cells were observed only in peripheral part of the pancreatic islets after 6 and 8 weeks of recovery phase. Expression of glucagon in liver decreased alongside; glucagon-positive cells were located predominantly in pericentral areas. Insulin-positive cells were found in central part of the pancreatic islets during the experiment. Insulin-positive hepatocyte-like cells were detected in the pericentral areas and in liver parenchyma from $4^{th}$ to $6^{th}$ weeks of diet, the number of these cells was the highest after 6 weeks of copper-deficient diet. After 8 weeks of diet we observed insulin-positive small round cells – at least 1 positive cell was around every tenth of central vein (these cells were single after 4 and 6 weeks of diet). Appearance of the insulin-positive hepatocyte-like cells was accompanied with increase of insulin level in venous blood. The maximum of insulin expression in liver coincided with the highest concentration of insulin in venous blood after 6 weeks of diet. After rats were transferred to normal rat chow, we observed solitary insulin-positive small round cells in liver tissue until $2^{th}$ week. Later positive cells were not detected in liver.

**Conclusion:** We suppose that glucagon-positive pancreatic islet cells are probably the source of pancreas regeneration in rat copper-deficient model; the appearance of glucagon- and insulin-positive cells in liver confirms common origin of these organs and can be the response reaction for the pancreatic tissue injury.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0085 A NEW ANIMAL MODEL IN PANCREATOLOGY- PANCREATIC DUCTAL FLUID AND BICARBONATE SECRETION IN WILD TYPE FERRETS

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**Introduction:** Cystic fibrosis (CF) is a lethal genetic disease affecting several organs, including the pancreas. Although animal models are available to study the CF-related tissue damage they have clear limitations. Recently a cystic fibrosis transmembrane regulator (CFTR) knock out ferret model was generated. This model would be the first available one to study pharmacological prevention of the disease development.

**Aims & Methods:** We aimed to characterize the fluid and bicarbonate secretion of wild type (WT) ferret pancreatic ducts. Expression of CFTR was detected by immunohistochemistry. Intra/interlobular pancreatic ducts were isolated from the WT ferret pancreas. Resting pH, buffer capacity and $Cl^-/HCO_3$ exchange activity were evaluated by microfluorometry. Fluid secretion was examined by video microscoopy.

**Results:** CFTR was expressed on the luminal membrane of ferret pancreatic ducts. The resting intracellular pH of pancreatic epithelial cells is lower ($7.17 \pm 0.08$) in ferrets compared to mice (7.31) or to guinea pigs (7.36). Concerning the bicarbonate influx mechanisms, functionally active sodium/hydrogen exchanger and sodium/bicarbonate cotransporter were detected. Anion exchanger activity measured by $NH_4Cl^-$ technique, $Cl^-$ removal and inhibitory stop methods indicated that ferret pancreatic ducts secrete similar amount of bicarbonate as mice and guinea pigs. Video microscopy revealed a significant increase in fluid secretion to $HCO_3^-$ and to 5 μM forskolin stimulation.

**Conclusion:** Ferret pancreatic ductal epithelial cells express the major epithelial ion transporters. Our results indicate that ferret could be a suitable model organism to study the CF-related pancreatic damage. Moreover this model opens up the possibilities to test pharmacological interventions in the disease development.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0086 CYCLIC ADENOSINE MONOPHOSPHATE PRODUCTION STIMULATED BY ORAI1 AND EXTENDED SYNAPTOTAGMIN 1

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**Introduction:** Cyclic adenosine monophosphate (cAMP) and $Ca^{2+}$ signaling play central role in the regulation of the secretory functions of epithelial cells. The two signaling system have multiple synergistic interactions helping to optimize the cellular response to stimulation. One of the interferences includes the interaction between the store operated $Ca^{2+}$ entry (SOCE) channel Orai1 with adenylyl cyclase 8 (AC8) that increase cAMP production, however its exact molecular mechanism is not known.

**Aims & Methods:** In this project we wanted to characterize the interactions of cAMP and $Ca^{2+}$ signaling further focusing on the molecular components of SOCE. Human embrional kidney (HEK) cells were transfected with plasmids encoding the proteins of interest. Cellular cAMP production was measured by fluorescence resonance energy transfer (FRET) using the cAMP reporter Epac1.

**Results:** The stimulation of the cells with 5 μM forskolin and 100 μM 3-isobutyl-1-methylxanthine (IBMX) resulted in reversible elevation in cAMP production. The expression of AC8 significantly elevated the cAMP response. Whereas, Orai1 induced spontaneous cAMP production and a massive increase in the stimulated cAMP production. The effect of Orai1 was completely $Ca^{2+}$ independent. Extended synaptotagmin 1 (E-Syt1), a recently described endoplasmic reticulum-plasma membrane tethering protein, increased the cAMP response, similarly to Orai1.

**Conclusion:** Our results showed that Orai1 and E-Syt1 play an important role in the regulation of cAMP production. However further studies are required to clarify the mechanisms of the interaction.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0087 VX-809 RESTORES THE EXPRESSION DEFECT OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR CAUSED BY ALCOHOL IN CAPAN-1 CELLS

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**Introduction:** Excessive ethanol consumption is one of the most common causes of acute and chronic pancreatitis. Earlier we showed that ethanol and ethanol metabolites cause severe damage in the function and expression of the cystic fibrosis transmembrane conductance regulator (CFTR), which increases the severity of acute ethanol-induced pancreatitis. There are new compounds available, such as lumacaftor (VX-809), to correct the impaired CFTR expression in cystic fibrosis patients, however the potential utility of this compound in pancreatitis treatment has never been investigated.

**Aims & Methods:** Our aim was to test the effect of VX-809 treatment on the CFTR expression during ethanol exposure. CFTR expression was evaluated by immunofluorescent staining in Capan-1 cells. The cells were incubated with 100 mM ethanol, 10 μM VX-809, or their combination for 24 h. Images were captured by confocal microscopy.

**Results:** As reported earlier exposure of Capan-1 cells to 100 mM ethanol for 24 hours significantly decreased the plasma membrane expression of CFTR. In parallel the cytoplasmic CFTR expression was increased. 10 μM VX-809 alone had no effect on the CFTR expression. Notably, application of 10μM VX-809 in pretreatment (treatment started 6 h prior to ethanol exposure), or post-treatment (treatment started 6 h after to ethanol exposure) significantly improved the plasma membrane expression of CFTR in Capan-1 cells.

**Conclusion:** These preliminary findings suggest that VX-809 might be able to restore the CFTR expression defect caused by alcohol. Further extended in vitro and in vivo studies need to clarify the effect of VX-809 on alcohol-induced pancreatic injury.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0088 MINIMALLY INVASIVE VERSUS OPEN NECROSECTOMY FOR NECROTIZING PANCREATITIS

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**Introduction:** Minimally invasive necrosectomy, as compared with open necrosectomy, may reduce death rates in patients with necrotizing pancreatitis, especially in critically ill patients.

**Aims & Methods:** We performed a registry study combining published and unpublished data from 15 cohorts of patients undergoing pancreatic necrosectomy in 65 hospitals in 8 countries. Death rates were compared in patients undergoing open necrosectomy or minimally invasive necrosectomy (i.e. minimally invasive surgical necrosectomy or endoscopic necrosectomy). We adjusted for confounding by three types of analyses: multivariable logistic regression, stratification according to the predicted risk of death at baseline (low: $<5\%$, intermediate: $\geq 5\%$ to $<15\%$, high: $\geq 15\%$ to $<35\%$ and very-high: $\geq 35\%$) and propensity-score matching.

**Results:** Among 1980 patients with necrotizing pancreatitis, 1167 underwent open necrosectomy, 467 underwent minimally invasive surgical necrosectomy and 346 underwent endoscopic necrosectomy. There was a lower risk of death for minimally invasive surgical necrosectomy (odds ratio, 0.53; 95%-CI, 0.34 to 0.84; $P=0.006$) and endoscopic necrosectomy (odds ratio, 0.19; 95%-CI, 0.06 to 0.61; $P=0.005$) as compared with open necrosectomy. After risk stratification and propensity-score matching, minimally invasive surgical necrosectomy remained associated with a lower risk of death than open necrosectomy in the very-high-risk group (risk ratio, 0.70; 95%-CI, 0.52 to 0.95; $P=0.02$). Endoscopic necrosectomy remained associated with a lower risk of death than open necrosectomy in the high-risk group (risk ratio, 0.27; 95%-CI, 0.08 to 0.88; $P=0.03$) and the very high-risk group (risk ratio, 0.43; 95%-CI, 0.24 to 0.77; $P=0.005$).

**Conclusion:** As compared with open necrosectomy, minimally invasive surgical or endoscopic necrosectomy for necrotizing pancreatitis reduces mortality among patients at high risk of death.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0089 THE FIRST MULTI-CENTRE EXPERIENCE FROM THE UK AND IRELAND OF THE USE OF THE HOT AXIOS SYSTEM FOR TRANSLUMINAL DRAINAGE OF PANCREATIC FLUID COLLECTIONS

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**Introduction:** Pancreatic fluid collections (PFC) are a common local complication of pancreatitis with incidences of 5–16% and 20–40% in acute and chronic pancreatitis respectively (1). Classification of PFC includes acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection and walled-off necrosis (WON). A new lumen-opposing, covered self-expanding metal stent on a catheter-based delivery system (Hot AXIOS, Boston Scientific) may have higher technical success rates, easier deployment and lower stent migration. We present the first multicentre prospective case series from the UK and Ireland to assess success and complication rates associated with Hot AXIOS stent for the drainage of PFC.

**Aims & Methods:** All adult patients who had Hot AXIOS stent placement for PFC from July 2015-February 2016 were included. Eight centres participated (London, Glasgow, Edinburgh, Newcastle, Cambridge, Manchester, Dublin and Leeds). All patients had CT assessment of the PFC prior to placement. Data including technical success, resolution of collection, complications and stent migration were collected.

**Results:** Forty patients were treated with a single Hot AXIOS stent in each case. The median age was 57 years (range 31–78) and 25 were male (63%). The indications were WON (24), pseudocyst (15) and abcess (1). The median size of the PFC was 10.9 cm (3.9–20 cm). Thirty-eight patients (95%) had trans-gastric stents, 1 had trans-duodenal and 1 had a trans-oesophageal stent. Thirty-seven (93%) had freehand puncture into the cyst, the rest were wire guided. Procedures were technically successful in all patients. Of 21 patients with available follow-up data to date, the collection resolved in 18 (86%) and reduced in size in 3 (14%). Twelve patients (30%) had 33 necrosectomies and/or endoscopic lavage following stent insertion. Stents migrated in 3 patients (7.5%). One patient developed small bowel obstruction resulting from stent migration and this was managed surgically. There was no procedure-related or 30-day mortality (data available in 27 patients).

**Conclusion:** This multicentre case series demonstrates that the Hot AXIOS system is safe and effective in draining PFC with a technical success rate of 100% and serious adverse event rate of 2.5%. The stent migration rate was 7.5%.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0090 RED CELL DISTRIBUTION WIDTH AND RATIO RED CELL DISTRIBUTION WIDTH/TOTAL SERUM CALCIUM AS MAJOR PREDICTORS OF SEVERITY AND MORTALITY IN ACUTE PANCREATITIS

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**Introduction:** Acute pancreatitis (AP) is associated with systemic inflammatory response syndrome and it has considerable mortality. The current severity scores include multiple variables, some of them only complete within 48 hours post-admission. Red cell distribution width (RDW) is a simple and routine parameter that seems to be related with inflammation.

**Aims & Methods:** To evaluate the diagnostic value of RDW in severity and mortality of AP. Retrospective case-control study of total of patients with severe AP (cases), between 2013 and 2015, who were compared with patients with mild AP (controls), in a proportion of 1:1. Additionally it was compared patients with AP that died (cases) with patients that not died (controls). The diagnosis and severity of AP were defined by modified Atlanta classification of 2012. Variables evaluated included demographics, comorbidities, laboratorial parameters, prognostic scores at the first 24 hours [Ranson, BISAP and Modified Marshall (MM)] and mortality.

**Results:** Registered 182 cases of AP. Included 91 cases of severe AP, 58.2% (n = 53) with male gender (vs 51.6%; p = 0.459) and mean age of 65.0 ± 16.3yo (vs 67.9 ± 13.7; p = 0.201). RDW was higher in patients with severe AP (14.6 ± 1.3 vs 12.7 ± 0.5; p < 0.001), as well as ratio RDW/serum calcium (1.8 ± 0.3 vs 1.3 ± 0.1; p < 0.001). After multivariate and ROC curve analysis, RDW (AUROC 0.959; p < 0.001) and RDW/serum calcium (AUROC 0.971; p < 0.001) were the major predictors of severe AP to a cut-off value of 13.0 (S-91.3%; E-95.6%) and 14.0 (S-91.3%; E-92.3%), respectively. These factors were superior to stablished prognostic scores as Ranson (AUROC 0.754; p < 0.001; cut-off: 3.0), BISAP (AUROC 0.735; p < 0.001; cut-off: 2.0) and MM (AUROC 0.772; p < 0.001; cut-off: 1.0). The mortality rate was 8.8% (16/182), all of cases associated with severe AP (17.6%; 16/91). RDW and RDW/serum calcium were superior in patients with AP that died (15.3 ± 1.4 vs 13.5 ± 1.3; p < 0.001 and 1.9 ± 0.3 vs 1.6 ± 0.3; p < 0.001, respectively). In multivariate and ROC curve analysis, the only independent risk factors mortality-associated in AP were RDW (AUROC 0.844; p < 0.001; cut-off: 14.0) and RDW/serum calcium (AUROC 0.830; p < 0.001; cut-off: 1.7).
**Conclusion:** RDW and serum calcium are simple and routine parameters, available in emergency department. This cohort showed that RDW and RDW/serum calcium are potential good predictors of severity and mortality in AP, being superior to conventional prognostic scores. RDW ≥ 13.0 and RDW/serum calcium ≥ 1.4 predict severe AP. RDW ≥ 14.0 and RDW/serum calcium ≥ 1.7 predict mortality in AP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0091 PREVALENCE OF POST-ERCP COMPLICATIONS ACCORDING TO HOSPITAL VOLUMES AND EXPERIENCE OF OPERATORS: A PROSPECTIVE MULTICENTER STUDY

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**Introduction:** Despite technical improvement and endoscopists' growing experience with ERCP procedures, the incidence of post-procedure pancreatitis has not yet dropped and efforts are still being made to identify factors associated with the risk and minimize the incidence and severity. Although patient- and procedure-related risk factors for post-ERCP pancreatitis were identified at previous studies, few studies were addressed the association between post-ERCP pancreatitis and endoscopists' experience and hospital's cases volume and showed a debate on the results.
**Aims & Methods:** The aim of our study was to evaluate the impact of endoscopist's experience and hospital's case volume on post-ERCP pancreatitis. Between January 2015 and August 2015, patients with naïve papilla who were referred for diagnostic and therapeutic ERCP were enrolled. Each endoscopist participated in the study entered the data for all consecutive ERCPs attempted and prospectively recorded details of patient- and procedure-related variables on data collection sheet at the time of ERCP. We analyzed the collected data for identifying patient- and procedure- related risk factors for post-ERCP complications and the impact of the endoscopist's experience (< 200 vs. > 200 cases of therapeutic ERCP) and the hospital's case volume (cutoff of 500 procedures per year) in a multicenter, prospective study in Daegu-Kyungpook Province.
**Results:** Data were obtained from 6 centers (four with high and two with low volume). A total of 883 patients (median age, 70 years; range, 19 ~ 101; male: female ratio, 1.34: 1) who underwent ERCP procedures were included in the study; 611 were performed in the 4 high-volume centers (69.2%) and 272 in the 2 low-volume centers (30.8%). Overall, 422 ERCPs were carried out by expert operators and 461 by less-experienced operators. Overall, post-ERCP pancreatitis occurred in 64 patients (7.3%). Post-ERCP pancreatitis was observed and classfied as mild in 56 (87.5%), moderate in 6 (9.4%) and severe in 2 (3.1%). The incidence of post-ERCP pancreatitis was lower in experienced endoscopist (3.3% vs. 10.9%, p < 0.001)). However, there was no difference according to hospital volume (high vs. low volume, 7.0% vs. 7.7%, p = 0.718).
**Conclusion:** Although our results revealed that the risk of post-ERCP pancreatitis was associated with the experience of endoscopist and not with hospital volume, further studies including larger samples and many hospitals with variable degree of case volume are needed to support our results and clarify risk factors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0092 EUS-GUIDED INTERVENTIONS FOR WALLED-OFF PANCREATIC NECROSIS: CLINICAL OUTCOMES OF A STEP-UP APPROACH AND RISK FACTORS FOR FAILED ENDOSCOPIC TREATMENT

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**Introduction:** Walled-off necrosis (WON) remains difficult to manage endoscopically because of insufficient drainage of solid necrotic debris. This study aimed to evaluate the technical/clinical success, and safety of EUS-guided treatment of WON and to ascertain factors associated with failed endoscopic treatments.
**Aims & Methods:** This retrospective study involved 70 consecutive patients who had undergone a step-up approach based on EUS-guided drainage for WON. Our treatment strategy is shown in Figure 1. Multivariable logistic regression analysis was performed to ascertain factors associated with failed endoscopic treatments.
**Results:** Seventy patients (57 men and 13 women; mean age 57.1 years) underwent EUS-guided drainage. Forty-one cases (59%) had a multilocular lesion and 13 cases (19%) had a WON cavity extending to the pelvis. The mean number of stents placed was 3.7; metal stents were deployed in 32 cases (46%). The technical success rate (successful stent deployment) of EUS-guided drainage was 97%. The clinical success rates (resolution of symptoms or inflammation) in STEP 1, 2, 3, and 4 were 40%, 69%, 76%, and 89%, respectively. Eight (11%) cases experienced adverse events related to endoscopic interventions and 10 (14%) required surgical necrosectomy; 8 (11%) patients died. The multivariable analysis for exploring factors associated with failure to manage the procedure successfully up to STEP 2 showed that ratios of patients with serious comorbidities (Charlson comorbidity index ≧ 3) and with WON cavity extending to the pelvis were the significant risk factors (odds ratio 5.3 and 4.7, P = 0.021 and 0.026, respectively).
**Conclusion:** A step-up approach based on EUS-guided drainage is an effective strategy for the management of WON, particularly in patients with serious comorbid conditions or in those with WON cavity extending to the pelvis, who are difficult to manage with endoscopy alone. More options, such as surgical necrosectomy should be considered.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0093 EVALUATION OF THE BISAP SCORE IN PREDICTING SEVERITY AND PROGNOSIS IF ACUTE PANCREATITIS

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**Introduction:** Early risk stratification of acute pancreatitis (AP) is essential to optimize the approach and improve outcomes. Among the several scoring systems, the index for severity in acute pancreatitis (BISAP) stands out for its versatility, including clinical, laboratory and radiological data. Only limited data is available regarding validation among different patient populations.
**Aims & Methods:** To evaluate the accuracy of the BISAP in predicting severe clinical outcomes in AP. Retrospective and single-center study, evaluating patients with AP. Outcomes: prolonged hospitalization (≥15 d), admission to intensive care unit (ICU), organ damage (PO2 ≤ 60 mmHg or need for ventilation; creatinine ≥2 mg/dl; systolic blood pressure ≤ 90 mmHg or need for vasopressor), its persistence (≥48 h), pancreatic necrosis and early (≤7 d) and late mortality (≥8 d). Accuracy was assessed separately according to etiology (lithiasic, alcoholic and non-lithiasic). Statistical analysis: SPSSv21.0.
**Results:** 198 patients, 69.2% male, mean age 58.5 ± 19.0 years. 56 patients (28.3%) were admitted to ICU and 19 patients (9.6%) died. BISAP was accurate in predicting pancreatic necrosis (AUC 0.74, p < 0.001), prolonged hospitalization (AUC 0.70, p = 0.001), need for ICU admission (AUC 0.88, p < 0.001), organ injury (AUC 0.61, p = 0.016), its persistence (AUC 0.72, p = 0.003) and early (AUC 0.95, p < 0.001) and late mortality (AUC 0.76, p = 0.008). Best cutoff value calculated for BISAP in predicting mortality was > 2 (sensibility 78.9%; specificity 86.7%). Separately, only in lithiasic and non-lithiasic pancreatitis could BISAP predict, with fair accuracy, persistent organ dysfunction (AUC 0.725 and 0.745, p = 0.03 respectively).
**Conclusion:** Overall, BISAP demonstrated high accuracy in all outcomes. This score is simple and easily allowing for early assessment of prognosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0094 DIAGNOSIS, MANAGEMENT AND CLINICAL OUTCOME OF ACUTE BILIARY PANCREATITIS IN HUNGARY – NATIONWIDE, MULTICENTER, RETROSPECTIVE ANALYSIS

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**Introduction:** Acute biliary pancreatitis (ABP) caused by gallstone disease is the most common form of acute pancreatitis. The role of endoscopic retrograde cholangiopancreatography (ERCP) in ABP is still controversial.
**Aims & Methods:** The study aimed to evaluate data on diagnosis, management and clinical outcome of ABP in Hungary. Retrospective clinical analysis of patients with ABP between January 2013 and August 2015 based on the National Pancreas Registry established by the Hungarian Pancreatic Study Group.
**Results:** Data of 371 patients with ABP including 210 (56.6%) females and 161 (43.4%) males with mean age of $61.7 \pm 18.1$ and $62.1 \pm 16.1$, respectively were evaluated. The diagnosis was made according to clinical symptoms, laboratory findings and/or clinical imaging. Cholelithiasis was detected in 74.1%, dilated common bile duct (CBD) in 32.6%, whereas choledocholithiasis in 5.1% by abdominal ultrasonography and/or computed tomography. According to laboratory tests biliary origin was determined in 42.3%. The majority of patients (67.7%) developed mild disease, 25.9% was identified as moderate and minority of cases (6.5%) was categorized as severe. In terms of therapy, ERCP was performed in 74.1%, in majority of patients (61.7%) during the first 24 hours after admission. During ERCP CBD stones were detected in 36.7%, CBD dilation in 45.8%. Endoscopic sphincterotomy was done in 86.5% and overall successful biliary clearance was achieved in 84.7%. According to Tokyo guidelines, definite cholangitis was assessed in 33.7%. In this group ERCP was performed in 84.8%, in 67% within 24 hours after admission. 62.3% of patients received at least 2000 ml of parenteral fluid during the first day, enteral feeding was administered in 27.8% (mostly in moderate or severe group) and antibiotics were given in 90.3%. Multimorbidity, age and length of hospital stay were associated with severity. Local complications developed overall in 29.3%, pancreatic necrosis in 12.4% and organ failure was identified in 7.8%. Mortality was 0.4%, 1.04% and 20.83%, respectively in mild, moderate and severe disease group. When ERCP was performed local or systemic complications developed in 27.6% or 6.9%, respectively compared to conservatively treated patients who developed local complications in 35.4% and systemic complications in 10.4%. Mortality was 1.5% in the ERCP treated group and 3.1% in conservatively treated group. Notable difference was assessed in patients with concomitant definite cholangitis where local complications developed in 25.5% vs. 36.8% and systemic complications in 3.8% vs. 10.5% when compared ERCP with conservative treatment. In patients where cholangitis was definitely ruled out the rate of complications and mortality was comparable between the ERCP and conservatively treated group.
**Conclusion:** ERCP is the mainstay of therapy of ABP in Hungary. The use of ERCP in ABP is associated with lower complication and mortality rate. Regardless of the treatment ABP is associated with significant morbidity and mortality. Registry provides comprehensive information which can help in further understanding and improving ABP management.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0095 IMPACT OF FATTY LIVER ON SEVERITY OF ACUTE PANCREATITIS

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**Introduction:** Acute pancreatitis is usually a mild disease; however, some patients may develop to severe courses. It is important to identify severe cases early because it enables early intensive care and nutritional support. Fatty liver change was commonly seen in patients with acute pancreatitis; however, its clinical significance have not been well studied.
**Aims & Methods:** We aimed to investigate the relationship between fatty liver and severity of acute pancreatitis. We retrospectively analyzed data from patients who were diagnosed with acute pancreatitis from July 2009 to June 2015. The unenhanced CT images were retrospectively reviewed by a radiologist and the mean hepatic and splenic attenuations were measured in Hounsfield units (HU). Fatty liver was defined as a mean hepatic/splenic HU $< 1$. The revised Atlanta classification was adopted to define the severity of acute pancreatitis.
**Results:** Among 167 patients, fatty liver was found in 57 patients (34.8%) and non-fatty liver in 107 patients (65.2%). Fatty liver was more frequently shown in male and obese patients. Compared with patients without fatty liver, the severity of pancreatitis and serum C-reactive protein levels were higher in fatty liver patients. Prevalence of local complications including pseudocyst and walled-off necrosis and mortality were higher in the patients with fatty liver. Even after adjusting for age, sex, body mass index, and cause of pancreatitis, fatty liver was significantly associated with moderately-severe or severe acute pancreatitis (odds ratio, 4.34; 95% confidence intervals, 2.00–9.40). Fatty liver was a poor prognostic factor not only in obese or alcoholic patients but also in non-obese or non-alcoholic patients.
**Conclusion:** Fatty liver may play a prognostic role in acute pancreatitis. Fatty liver can be usefully incorporated into future predictive scoring models.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0096 MIR 210-3P AND MIR 10B-5P AS A POTENTIAL BIOMARKERS FOR DIFFERENTIATION BETWEEN CHRONIC PANCREATITIS AND PANCREATIC CANCER

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**Introduction:** Chronic pancreatitis (CP) is a chronic inflammatory disease of pancreas characterized by irreversible morphological changes providing to exocrine and endocrine dysfunction. It's known that CP is a main risk factor of pancreatic cancer (PC). A number of studies have been performed in order to identify biomarkers for this disease. Recently, microRNAs (miRNAs), short, non-coding RNAs have been proposed as possible biomarkers. Several miRNAs were found to be associated with malignant processes.
**Aims & Methods:** The aim of our study was identification of miRNAs that could be markers for differentiation between CP and PC. We assessed expression of selected miRNAs, as well as parameters in serum including lipase, amylase, bilirubin, aminotransferases activity, gamma glutamylotranspeptidase, alkaline phosphatase activity, CRP and Ca 19-9. Blood samples from patients with CP (34) and PC (26) were collected in Department of Gastroenterology with Endoscopic Unit, Medical University, Lublin. RNA was extracted from serum using miRCURY RNA Isolation Kit Biofluids and reverse transcribed using the Universal cDNa Synthesis Kit, according to the manufacturer's protocol. Diluted cDNA was mixed with microRNA LNA primers and SYBR Green Master Mix. Assay was performed in triplicate, and the expression levels of miRNAs were quantified using LightCycler 480® II following the manufacturer's instruction. We screened the expression level of five microRNAs (miR-30c, miR-103a, miR-124-3p, miR-191, miR-423-3p) and selected miR-103a as a reference gene with the minimal variation between the two groups. The relative expression of miRNAs was calculated using the comparative cycle threshold ($\Delta\Delta$CT) method. Nonparametric tests (Mann-Whitney and Spearman) were used for statistical analysis.
**Results:** We observed significantly higher expression of miR 210-3p in PC than in CP ($p = 0.015$) and lower but not statistically significant expression of miR 10b-5p. We also found statistically significant correlation between alkaline phosphatase and miR 210-3p ($p < 0.02$), between miR 210-3p and gamma glutamylotranspeptidase ($p < 0.02$), miR 10b-5p and CRP ($p < 0.04$) in patients with PC. On the other hand statistically significant difference was observed between miR 10b-5p and Ca 19-9 ($p < 0.005$) in patients with CP.
**Conclusion:** We can conclude, that two of investigated microRNAs: miR210-3p and miR 10b-5p may be take into consideration as possible biomarkers for differentiation between CP and PC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0097 PANCREATIC ENDOCRINE FUNCTION IN PATIENTS WITH CHRONIC PANCREATITIS: EVALUATION AND RELATION TO MALNUTRITION

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**Introduction:** Chronic pancreatitis (CP) progression leads to pancreatic endocrine and exocrine dysfunctions. We evaluated Diabetes Mellitus type 3c (DM) presence in patients (pts) with CP and assessed the endocrine function relation with pancreatic exocrine insufficiency (PEI) and with pre-albumin (transthyretin, TTR) and retinol-binding protein (RBP) as markers for malnutrition.

**Aims & Methods:** Serum samples of 106 pts (55 male, 51 female) were collected in our centre for the period February 2014 – January 2016. We divided all patients into 3 subgroups: subgroup 1- CP without DM (68pts); subgroup 2- CP with DM (18 pts); subgroup 3- control group (20 pts). Patients were also subdivided according to Cambridge classification for CT/MRCP - grade 1–4. Serum TTR and RBP levels were measured by immunonephelometry assay. Endocrine function was evaluated using fasting levels of HBA1C, glucose (mmol/L), Insulin (method ECLIA ref. range 3–20$\mu$U/ml) and C-peptide (method ECLIA ref. range 1.1–4.4 ng/ml). Based on their results HOMA1, HOMA2[1] indices and FCGR (fasting C- peptide/ glucose ratio) were calculated for assessment of insulin secretion and insulin sensitivity. The used below HOMA1-IR and HOMA2%$S_{insulin}$ (markers for insulin sensitivity) were calculated via glucose and insulin levels, and HOMA2%$B_{c\text{-}peptide}$ (marker for insulin secretion) and FCGR- via C-peptide and glucose levels. Exocrine function was evaluated using faecal elastase-1 (FE-1: cut-off for PEI $< 200\,\mu$g/g). The statistical analysis was performed applying SPSS version 22.

**Results:** By subgroup 3 we observed glucose median 5.0, Insulin 7.2, C-peptide 1.8, HOMA1-IR 1.6, HOMA2%$S_{insulin}$ 99.7 and HOMA2%$B_{c\text{-}peptide}$ 103.9, which indicated normal insulin secretion and sensitivity. Subgroup 2 was with the lowest levels of C-peptide 0.68, HOMA2%$B_{c\text{-}peptide}$ 33.4, FCGR10.7, associated with low insulin secretion, and the highest levels of HOMA2%$S_{insulin}$ 154, related to high insulin sensitivity, with significant differences in values compared to other subgroups, $p < 0.05$. Within subgroup 1, 14 pts were with HOMA1-IR $> 2$ and their data demonstrated high insulin secretion (HOMA2%$B_{c\text{-}peptide}$ 158.5) and low insulin sensitivity (HOMA2%$S_{insulin}$51.9) with significant differences to all other subgroups, $p < 0.05$. By the rest 54 pts within subgroup 1, we observed significantly lower C-peptide, Insulin, HOMA2%$B_{c\text{-}peptide}$ and FCGR within CT/MRCP grade 3 and 4, $p < 0.05$. TTR for all pts were $0.24 \pm 0.09$ g/L and RBP $0.039 \pm 0.014$. TTR under 0.2 g/L were found in 33% in subgroup 1 and in 11 pts in subgroup 2; RBP under 0.03 g/L - in 35.3% in subgroup 1 and in 9 pts in subgroup 2, with significant differences in mean values in both subgroups, $p < 0.05$. Within both CP groups PEI was found in 30 pts. Levels of HOMA2%$B_{c\text{-}peptide,}$ reflecting insulin secretion, were lower in pts with PEI, $p < 0.05$. Within levels of C-peptide (below 1.1 ng/ml) there was a relation between TTR levels and PEI presence $\chi^2 = 4.6$, $p = 0.035$, with Odd Ratio 2.9 (95%CI 1.1–7.1).

**Conclusion:** PEI and malnutrition with lower TTR and RBP levels have closely related to the pancreatic endocrine function in CP patients which requires establishing insulin status. DM type 3c has negative impact on malnutrition in CP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0098 RELATION BETWEEN VITAMIN D STATUS AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH CHRONIC AND RECURRENT PANCREATITIS - PRELIMINARY DATA

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**Introduction:** Deficiency of fat-soluble vitamin D (VD) is a present complication in pancreatic disorders. Studies have demonstrated that low VD levels may be associated with increased cardiovascular risk (CVR) and adverse cardiovascular events.

**Aims & Methods:** To assess the relation between VD levels and CVR factors by patients (pts) with chronic pancreatitis (CP) and reccurent pancreatitis (RP). Study enrolled 66 pts (38 males, mean age 49.8yrs): 40 pts had CP and 26-RP. Determination of 25-hydroxyvitamin D (25OHD, sum of 25OHD3 and 25OHD2) was performed by a validated, DEQAS certified ID-LC-MS/MS method with accuracy and precision within 7.5% and linearity range 3.0–300.0 nmol/L. VD status was assessed as deficiency (25OHD $< 25$ nmol/L), severe insufficiency (25–50 nmol/L), mild insufficiency (50–80 nmol/L), and sufficiency ($> 80$ nmol/L). CVR was investigated by European SCORE chart (Systematic COronary Risk Evaluation) and was calculated as percent for the 10-year risk mortality; CVR factors- by lipid profile, apolipoproteins A and B, CRP, fasting glucose levels (FGL), diabetes mellitus (DM), blood pressure; imaging morphological data- by Cambridge classification for CT/MRCP (grade I-IV); pancreatic exocrine insufficiency (PEI)- by fecal elastase-1 (cut-off for PEI $< 200\,\mu$g/g). Statistical analysis was performed via SPSS v22.

**Results:** Total 25OHD for all pts was $41.47 \pm 26.36$ nmol/L (range 3.81–93.8 nmol/L); 23 pts (34.8%) had deficiency; profound insufficiency was found in 27.3% of pts; another 31.8% were with mild insufficiency, and only 4 pts (6.1%) were in sufficiency status. According to SCORE, 7.6% had low ($<1$%), 50%-moderate ($\geq 1$ and $<5$%), 18.2%-high ($\geq 5$% and $<10$%) and 24.2%-very high ($\geq 10$%) risk for CVD-events that eventually will occur after 10 years. Patients with PEI compared to pts without PEI had higher CVR based on SCORE chart results, $p < 0.05$. Among pts with severe morphological changes (grade III and IV, $n = 36$ pts), SCORE results were as follows: 30.6% had very high, 25%-high, 33.3%-moderate and 11.1%-low CVR, which was significantly higher compared to pts with mild structural changes (grade I and II), $p < 0.05$. VD status worsened with increasing the 10-year risk mortality (moderate, high and very high), $p < 0.05$. Lower VD levels were associated with higher FGL and DM ($22.52 \pm 13.10$ vs. $44.84 \pm 26.76$ nmol/L), $p < 0.05$. There was statistically significant correlation between VD levels and triglycerides (TG) and VLDL, $p < 0.05$. CRP correlated with increased cholesterol and decreased VD levels, which were lower by pts with RP, $p < 0.05$. We found no significant relation between VD levels and gender; systolic and diastolic blood pressure.

**Conclusion:** We confirmed a high prevalence of VD insufficiency and deficiency in CP and RP patients, related to impaired pancreatic structure and exocrine function. VD status was associated with the presence of increased CVR assessed by SCORE chart and CVR factors (DM, FGL, TG, VLDL, CRP). Further studies are required to establish CVR screening panel in this population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0099 GENOME ANALYSIS WITH WHOLE EXOME SEQUENCING TO IDENTIFY GENETIC ALTERATIONS IN PATIENTS WITH IDIOPATHIC PANCREATITIS

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**Introduction:** Idiopathic pancreatitis (IP) is designated to cases of pancreatitis wherein a diagnosis could not be made through routine evaluations including a thorough history, physical examination, laboratory studies and imaging modalities. Genetic alterations are known to be one of the most important etiologies in patients with IP. However, researches for related genes were conducted mostly in the Western countries and data is limited in the Asian population.

**Aims & Methods:** To reveal possible ethnic difference, genome analysis with whole exome sequencing was performed in Korean patients with IP. Patients who met the diagnostic criteria and provided written informed consent were enrolled consecutively at 8 university hospitals in the Metropolitan Seoul between March 2015 and February 2016. Blood samples were transferred to and analyzed at a single laboratory (the Genome Institute of MACROGEN, Inc.).

**Results:** The results from 18 patients with IP were compared with those from 7 patients with alcoholic chronic pancreatitis as the control group. In the IP group, alteration in ADRBK1 (adrenergic beta receptor kinase 1) gene was the most prevalent (12/18, 66.7%), followed by CDC34 (cell division cycle 34) (11/18, 61.1%) and CHRNA7 (cholinergic receptor nicotinic alpha 7 subunit) (11/18, 61.1%). There was no alteration for these genes in the control group. Interestingly, any alterations in established genes including PRSS1 (Protease, serine 1), PRSS2 (Protease, serine 2), SPINK1 (Serine peptidase inhibitor, Kazal type), CTRC (Chymotrypsin C), CASR (Calcium sensing receptor) and CPA1 9 Carboxypeptidase A1) were not detected in both groups.

**Conclusion:** ADRBK1, CDC34 and CHRNA7 may serve as new candidates for the hot spots in patients with IP. Also, there may be an ethnic difference in the genes associated with the heredity of pancreatitis. Further validation studies to explain the association between the genetic alterations in above genes and IP are anticipated in the future.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0100 PREVALENCE OF EXOCRINE PANCREATIC INSUFFICIENCY IN PATIENTS WITH CHRONIC PANCREATITIS WITHOUT FOLLOW-UP: NUTRITIONAL STATUS AND QUALITY OF LIFE. PANCR-EVOL STUDY

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**Introduction:** Exocrine pancreatic insufficiency (EPI) is an important complication of chronic pancreatitis (CP). (1) Guidelines recommend to rule out EPI in CP, to detect those patients who would benefit from pancreatic enzyme replacement therapy. (2).

**Aims & Methods:** The aim of this study was to evaluate the prevalence of EPI in patients with CP without follow-up in the last 2 years and to describe their nutritional status and quality of life (QoL). This was a cross-sectional Spanish multicenter study. We included patients with CP, without follow-up by a gastroenterologist or surgeon in at least 2 years. The exocrine function was evaluated in these patients. EPI was defined as a fecal elastase (FE) test $<200$ mcg/g. For nutritional assessment, laboratory and anthropometric data were obtained. QoL was investigated using the EORTC QLQ-C30 questionnaire

**Table 1:** Baseline characteristics.

| | Study population (n = 64) | EPI group (N = 41) | Non-EPI group (N = 23) | P value |
|---|---|---|---|---|
| Men | 55 (85.9%) | 36 (87.8%) | 19 (82.6%) | 0.7109 |
| Caucasic Race | 63 (98.4%) | 41 (100.0%) | 22 (95.7%) | 0.3594 |
| Age (years) | 58.8 (10.3) | 58.6 (9.0) | 59.0 (12.4) | 0.8799 |
| BMI (kg/m$^2$) | 24.5 (3.3) | 23.9 (3.5) | 25.7 (2.5) | 0.0334 |
| Time since diagnosis of CP (months) | 58.7 [37.7, 95.4] | 62.1 [39.0, 104.9] | 55.8 [35.4, 78.2] | 0.7487 |
| Pancreatic calcifications | 42 (65.6%) | 27 (65.9%) | 15 (65.2%) | 1.0000 |
| Biliary duct dilation | 40 (62.5%) | 28 (68.3%) | 12 (52.2%) | 0.2142 |
| Bowel movements/day | 2.0 [1.0, 2.0] | 2.0 [1.0, 3.0] | 1.0 [1.0, 2.0] | 0.0603 |
| Diabetes | 29 (45.3%) | 25 (61%) | 4 (17.4%) | 0.0008 |
| **Smoking habit** | | | | |
| Smokers | 41 (64.1%) | 28 (68.3%) | 13 (56.5%) | 0.6937 |
| Cigarettes per day | 20 [15, 30] | 20 [13.5, 25] | 20 [20, 30] | 0.3639 |
| **Alcohol consumption** | | | | |
| Habitual | 34 (53.1%) | 23 (56.1%) | 11 (47.8%) | 0.0372 |
| Ex-alcoholic | 18 (28.1%) | 14 (34.2%) | 4 (17.4%) | |
| Grams of alcohol/day | 60 [40, 90] | 61.5 [40, 87] | 60 [30, 100] | 0.9155 |

**Results:** 64 patients (see baseline characteristic, table 1) from 10 centers were prospectively included. 64.1% patients were tested positive for EPI (FE $<200$ mcg/g) and 45.3% of them had severe EPI (FE $<100$ mcg/g). Regarding nutritional status, the following differences were observed (EPI vs. Non-EPI): BMI ($23.9 \pm 3.5$ kg/m$^2$ vs. $25.7 \pm 2.5$, $p = 0.03$); glucose (121 [96, 189] mg/dl vs. 98 [90, 116]; $p = 0.006$); HbA1c 6.6% [6.0, 8.4] vs. 5.5 [5.3, 6.0] $p = 0.0005$); Vitamin A (0.44 mg/l [0.35, 0.57] vs. 0.53 [0.47, 0.63] $p = 0.048$) and Vitamin E ($11.2 \pm 5.0$ mg/ml vs. $14.4 \pm 4.3$, $p = 0.03$). EPI group showed a worse EORTC QLQ-C30 score on physical (93.3 [66.7, 100] vs. 100 [93.3, 100], $p = 0.048$) and cognitive function (100 [83.3, 100] vs. 100 [100, 100], $p = 0.04$). Other frequent complications of CP apart from EPI were: pseudocysts, chronic abdominal pain, biliary obstruction and splenic vein thrombosis.

**Conclusion:** Prevalence of EPI is high in patients with CP without follow-up**.** EPI group vs non-EPI group had significative lower BMI, higher levels of glucose, Hba1c, lower of vitamins A, E and a worse QoL.Regular follow up should be attempted; in this study we have used fecal elastase, an easy screening method.

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E. Marín: E. Marin has given lectures sponsored by Mylan partially related with the submitted work.
M. Francisco González: M. Francisco has given lectures sponsored by Mylan partially related with the submitted work.
E. Martínez-Moneo: E. Martinez-Moneo has given lectures sponsored by Mylan partially related with the submitted work.
A. Del Pozo-García: A. del Pozo has given lectures sponsored by Mylan partially related with the submitted work.
E. Pérez Rodríguez: She has given lectures sponsored by Mylan partially related with the submitted work.
E. Labrador: E. Labrador is employee of Mylan.
M.L. Orera Peña: Maria Luisa Orera is employee of Mylan.
E. De Madaria: Enrique de-Madaria has received a grant from Abbott and has consulted Mylan in the development and performance of clinical research in pancreatic exocrine insufficiency.
All other authors have declared no conflicts of interest.

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## P0101 CLINICAL FEATURES OF ACUTE OBSTRUCTIVE SUPPURATIVE PANCREATIC DUCTITIS: A RETROSPECTIVE REVIEW OF 20 CASES

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**Introduction:** The concept of acute obstructive suppurative pancreatic ductitis (AOSPD) has been proposed recently. It is characterized by a purulent discharge from the distal part of the duct without evidence of any infected necrotic tissue or coexisting pancreatic abscess. However, AOSPD has not been recognized sufficiently because of its rarity.

**Aims & Methods:** We aimed to clarify the clinical features of AOSPD. We retrospectively reviewed the clinical features of 20 patients with AOSPD at two tertiary referral centers between 1993 and 2012. We compared 17 AOSPD patients with chronic pancreatitis (CP) and 42 patients with acute-on-CP in terms of clinical characteristics, presentation, and laboratory and imaging findings.

**Results:** The etiology of AOSPD involved CP in 17 (85%) patients, pancreatic ductal adenocarcinoma in 2 (10%), and intraductal papillary mucinous neoplasm in 1 (5%). Endoscopic pancreatic drainage was effective in 19 (95%) patients. Body temperature was significantly higher in AOSPD with CP than acute-on-CP patients (median: 38.2 vs. 36.9°C; $p < 0.001$). Serum amylase levels at onset were significantly lower (median: 133 vs. 364.5 U/L; $p = 0.009$), and C-reactive protein was significantly higher (median: 9.42 vs. 1.06 mg/dL; $p < 0.001$) in AOSPD with CP patients. Enlargement of the pancreatic parenchyma (18% vs. 93%; $p < 0.001$) and stranding of the surrounding fat (12% vs. 93%; $p < 0.001$) on computed tomography were observed less frequently in patients with AOSPD with CP patients. The diameter of the main pancreatic duct was significantly greater in AOSPD with CP than acute-on-CP patients (median: 7 vs. 5 mm; $p = 0.006$).

**Conclusion:** The major etiology of AOSPD involved CP, and endoscopic pancreatic drainage was effective. The clinical features differ between AOSPD with CP and acute-on-CP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0102 THE INFLUENCE OF ERYTHROPOETIN ON APOPTOSIS AND FIBROSIS IN CHRONIC CERULEIN – INDUCED PANCREATITIS IN RATS

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**Introduction:** Chronic pancreatitis (CP) is a continuing, inflammatory process of the pancreas, characterized by irreversible morphological changes. The identification of pancreatic stellate cells resulted in the development of research on the pathogenesis of CP. The intensity of fibrosis depends on the production of extracellular matrix components and their degradation by metalloproteinases (MMP) - zincdependent endopeptidases. Gelatinases (MMP-2 and MMP-9) play the most important role in inflammatory processes because of their ability to degrade type IV collagen. Erythropoietin (EPO) regulates the interaction between apoptosis and inflammation of the brain, kidney and heart muscle. Epo receptors were also found in the pancreas, in particular the islet cells.
**Aims & Methods:** Our objective was to evaluate the influence of erythropoetin on fibrosis and apoptosis in experimental chronic pancreatitis. The experiments were performed on 48 Male Wistar rats (250–350 g). The animals were divided into six equal groups. (I – control, II – chronic cerulein – induced pancreatitis, III - erythropoetin s.c. (5 doses - 1 ml Epo/day), IV - erythropoetin s.c. (5 doses - 0.5 ml Epo/day), V – CP treated with 1 ml Epo, VI – CP treated with 0.5 ml Epo. The animals were sacrificed after 24 hours from the administration of the last doses. The blood for gelatinases and pancreas for the morphological examinations and immunohistochemistry were collected. MMP-2 and MMP-9 activities in serum were determined with gelatin zymography. groups. Histological changes of the pancreas were classified, based on the approximate percentage of acinar cells showing vacuolization, edema, and the areas showing inflammatory cell infiltration and fibrosis: 0 = absent, 1 = < 5%, 2 = 5–25%, 3 = 25–50%, 4 = > 50%.
**Results:** In the groups receiving cerulein injections the intensification of fibrosis around the pancreatic ducts was observed. Comparably, a slight reduction of interstitial edema and less severe fibrosis were reported in the groups treated with Epo. In group II, a strong expression of $\alpha$-actin was noticed in damaged acinar cells and the cells with vacuolar degeneration. The $\alpha$-actin expression appeared focally in groups V and VI, mostly in cells with the vacuolar degeneration, and is not visible in cells with inflammatory changes. In group II there was a very weak expression of Bcl-2 in acinar cells, while in the other groups, there was no expression noted. In group II cytoplasmic expression of caspase-3 was observed in the acinar cells, especially in the inflammatory changes and the cells with vacoular degeneration. In groups V and VI a reduced expression of caspase-3 was observed in areas with inflammation. In the cells with vacuolar degeneration, a weak, focal expression was noticed. There were no statistically significant differences between the groups in the activity of gelatinases.
**Conclusion:** Conclusions: Erythropoietin seems to have the effect of reducing fibrosis and apoptosis in an experimental model of chronic pancreatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0103 COMPARISON OF REMNANT-INVAGINATION AND DUCT-TO-MUCOSA PANCREATICOJEJUNOSTOMY FOLLOWING WHIPPLE'S RESECTION: PROSPECTIVE RANDOMIZED TRIAL IN PATIENTS AT HIGH RISK OF POSTOPERATIVE PANCREATIC FISTULA

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**Introduction:** Pancreatitis and pancreatic fistula following pancreaticoduodenectomy (POPF) are potentially lethal postoperative complications that may occur after extensive surgical manipulation of viable pancreatic parenchyma[1, 2]. The aim of this clinical trial was to evaluate the outcomes of a remnant-invaginating pancreatojejunal reconstruction technique (RI) in a patient cohort at high risk for POPF, and to compare it to the traditional duct-to-mucosa anastomosis technique (DM) regarding the risk of associated morbidity.
**Aims & Methods:** This prospective randomized clinical trial was conducted between 2012-15 in patients undergoing pancreaticoduodenectomy. Eligible candidates were identified by radiological criteria at the multidisciplinary pancreatic conference[3]. The POPF risk was estimated intraoperatively according to a previously published standardized assessment[4]. Patients who were assessed to have a high risk of POPF were included in the trial and randomized to either RI or DM. POPF and associated morbidity were classified according ISGPF[5] and Dindo-Clavién[6].
**Results:** One hundred and twenty consecutive high-risk patients were included into the analysis (60 RI, 60 DM). Pancreatic duct diameter and pancreatic gland circumference were median 2 and 80 mm, respectively. The RI and DM groups had comparable outcomes regarding duration of surgery (median 336 min) and blood loss (median 400 mL). The RI reconstruction took less time (28 min) to complete compared to the DM reconstruction (36 min; $p = 0.001$), but caused more technical problems (RI 14 patients, DM 7 patients). Severe postoperative complications were observed in 57 patients (48%; RI 25 patients, DM 32 patients; $p = 0.273$). Overall mortality was 7.5% (9 patients; RI 2 patients, DM 7 patients; $p = 0.163$), POPF-associated mortality was 5% (6 patients; RI 1 patient, DM 5 patients; $p = 0.207$). Clinically-relevant POPF (POPF B or C) was observed in both groups (RI 30 patients, DM 31 patients); however, the RI group had significantly fewer cases of severe POPF (POPF C; 2 patients; 3.3%) compared to DM (12 patients; 20%; $p = 0.008$).
**Conclusion:** The results of this prospective randomized trial indicate that the described remnant-invaginating pancreaticojejunostomy represents a suitable technique for safe pancreatojejunal reconstruction following Whipple's resection. In high-risk patients with soft pancreatic parenchyma and small pancreatic duct, the remnant-invaginating technique was associated with a lower risk of severe postoperative pancreatic fistula than the traditional duct-to-mucosa technique.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0104 THE EFFICACY AND SAFETY OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) FOR PANCREATIC SOLID MASS LESIONS: A PROSPECTIVE MULTICENTER COHORT STUDY IN JAPAN

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**Introduction:** EUS-FNA for pancreatic solid mass lesions is important because of its high diagnostic yield. Multicenter prospective studies have established the clinical efficacy of EUS-FNA for pancreatic solid mass lesions, however prospective studies in Japan are lacking.
**Aims & Methods:** The aim of the study is to evaluate the efficacy and safety of EUS-FNA for pancreatic solid mass lesions in a multicenter study based in Japan. The primary outcome measure was the diagnostic sensitivity by EUS-FNA. The secondary outcomes were specimen adequacy, diagnostic yield, adverse events and diagnostic accuracy related to the procedure. Diagnostic yield was defined by the percentage of lesions sampled for which a tissue diagnosis was obtained. Specimen adequacy was defined as the percentage of lesions sampled in which obtained material was representative of the target site and sufficient for diagnosis. Patients were prospectively enrolled and EUS-FNA was performed. All procedures were performed by experienced endoscopists who have performed at least 100 cases or by less-experienced endoscopists assisted by such experienced endoscopists. Data related to EUS guided tissue acquisition in addition to white blood cell count (WBC), hemoglobin (Hb), serum c-reactive protein (CRP) and serum pancreas-related amylase (p-AMY) between pre- and post-examination were collected. Adverse event rates were determined within 24 hours and after 7 and 28 days. After pathological evaluation, the collected specimens were interpreted as benign, malignant, or non-diagnostic specimens. Diagnostic accuracy was then determined and defined as the percentage of lesions sampled by EUS that correspond to the final histopathologic diagnosis at surgery or clinical follow up of 1 year.
**Results:** Two hundred and forty-nine patients were enrolled from November 2011 to June 2013. One patient suffered from cerebral infarction just before procedure. In 2 patients, EUS could not detect target lesions. Therefore, these 3 cases were excluded. A median of 2 passes were performed per procedure. In 99 cases (40.2%), specimens were evaluated immediately by pathologists, cyto-techinicians or endoscopists trained in cytopathology. The specimen adequacy rate was 100% in 246 cases. From these specimens, 215 cases were diagnosed as malignant lesions, 27 cases were diagnosed as benign, and 4 cases were non-diagnostic. The diagnostic yield was 98.4% (242/246). There was no significant difference in WBC, Hb, CRP, p-AMY between pre- and post-examination. The complication rates within 24 hours and after 7 and 28 days were 2.8%, 1.6% and 0% respectively. After 1-year follow up, 7 cases interpreted as malignant by EUS-FNA were lost for follow up and excluded for final evaluation. Finally, diagnostic sensitivity, specificity, accuracy, positive predictive value and negative predictive value were 97.2% (208/214), 88.0% (22/25), 96.2% (230/239), 100% (208/208), 81.4% (22/27), respectively based on final histopathology at the time of surgery or clinical follow up period of 1 year.

Pathological diagnosis and final diagnosis

| | Final diagnosis | | | | |
|---|---|---|---|---|---|
| Malignant | | Benign | Unknown | Total | |
| Pathological diagnosis | Malignant | 208 | 0 | 7 | 215 |
| | Benign | 5 | 22 | 0 | 27 |
| | Non-diagnostic | 1 | 3 | 0 | 4 |
| | Total | 214 | 25 | 7 | 246 |

**Conclusion:** EUS-FNA for pancreatic solid lesions has a high diagnostic yield and is a safe procedure in Japan consistent with previously published international studies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0105 ECHOENDOSCOPIC ETHANOL ABLATION OF TUMOR COMBINED TO CELIAC PLEXUS NEUROLYSIS IN PATIENTS WITH PANCREATIC ADENOCARCINOMA

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**Background:** Endoscopic ultrasonography (EUS) guided-celiac plexus neurolysis (EUS-CPN) has proven able to relieve pain in pancreatic cancer (PC) patients, but with often suboptimal and transient results. The study is aimed at comparing the efficacy and safety of EUS-guided tumor ethanol ablation combined to CPN with respect to EUS-CPN alone for pain management in PC patients.
**Methods:** Among 123 unresectable PC patients referred to our Institution between 2006 and 2014, 58 treated with EUS-CPN (group 1) and 65 with the combined approach (group 2) were compared. Logistic regression models were applied to identify predictors of pain relief, while time-to-event data were compared by means of log-rank test.
**Results:** The two groups presented similar baseline clinical and tumoral parameters. Pre-procedural visual analogue scale (VAS) score was 7 in both groups ($p = 0.8$) and tumor max diameter was 38 mm (range 25–59) in group 1 and 43 mm (22–59) in group 2 ($p = 0.4$). The combined treatment increased the pain relief and the complete pain response rate ($p = 0.005$ and 0.003, respectively). Median duration of pain relief was 10 (7–14) and 18 (13–20) weeks in the two groups, respectively ($p = 0.004$). At multivariate regression, initial VAS score and EUS technique adopted resulted significantly associated to pain relief. No severe treatment-related adverse events were reported. Median overall survival was 6.5 months (5.1–8.6) in group 1 and 8.3 months (6–11.4) in group 2 ($p = 0.05$).
**Conclusion:** EUS-guided tumor ablation combined to CPN appears to be superior to standard EUS-CPN in terms of pain control and overall survival.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0106 INTRAOPERATIVE US IS THE MAIN TOOL FOR MAKING DECISION ON ARTERIAL RECONSTRUCTION DURING DP-CAR. EXPERIENCE OF 20 MODIFIED APPLEBY PROCEDURES

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**Introduction:** Distal pancreatectomy with celiac artery resection (DPCAR) is widely used for borderline-resectable pancreatic cancer. It is believed that considerable reduction of the liver arterial supply after DPCAR may cause severe liver dysfunction and/or gallbladder necrosis. The decision to reconstruct artery or not is still difficult.
**Aims & Methods:** To study liver collateral arterial supply after temporary occlusion of the common (CHA), right gastroepiploic (RGEA) and accessory/replaced left hepatic arteries (a/rLHA). Arterial anatomy, diameters of CHA, proper hepatic (PHA), gastroduodenal (GDA) and pancreatoduodenal arteries (PDA) were registered before surgery in 110 consecutive patients with pancreatic body/tail cancer (n35), gastric cancer with pancreatic involvement (n30) and liver tumors (n45) by CT. For DPCAR (n20) these data were obtained after surgery as well. Diameters of peripancreatic arteries and mean systolic blood velocity in hepatic arteries before and after CHA clamping were measured intraoperatively by Doppler ultrasound.
**Results:** Classical arterial anatomy was identified in 67% and replaced right hepatic artery (rRHA) from the SMA in 12.2% of cases. Pulse had disappeared in 19 (17%) cases after clamping of CHA, RGEA and aLHA/rLPA. Collateral arterial blood flow in the liver parenchyma was revealed in all cases. DPCAR led to increase of GDA, rRHA, PDA and RGEA blood flow in 0.9–2 times; visualization of PD arcades as a main and sole collateral way after DPCAR.
**Conclusion:** Doppler ultrasound is a good modality for intraoperative assessment of liver arterial blood supply after DPCAR; Hepatic artery reconstruction may be necessary after DPCAR in case of disappearance of arterial Doppler signal upon the liver parenchyma.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0107 PANCREATIC CANCER IN PATIENTS WITH AUTOIMMUNE PANCREATITIS: A SCOPING REVIEW

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**Introduction:** Autoimmune pancreatitis (AIP) is a rare chronic inflammatory disease of the pancreas which responds well to immunosuppressive therapy. As its manifestation often mimics pancreatic cancer (PDAC), a lot of attention has been given to differentiation of the two conditions.
Chronic inflammatory process is a well-known risk factor of malignancy, as described in chronic pancreatitis and PDAC. A similar association in patients with AIP and PDAC has been suggested but not clearly demonstrated.

**Aims & Methods:** The aim of our study was to identify and analyze all published cases of AIP and PDAC co-occurrence focusing on the interval between the two diagnoses and the location of the PDAC lesions.
Studies were identified by searching MEDLINE, EMBASE, Scopus and Web of Science databases. The computer search was supplemented with manual searches for reference lists of all retrieved articles.
**Results:** Forty-five cases of PDAC in AIP patients (1 certain and 8 potential duplicates) were reported in 10 case reports, 1 case-control study, 13 retrospective and 5 prospective cohort studies. The interval between the diagnoses of AIP and PDAC was stated in 22 studies (30 unique cases, 1 duplicate). Synchronous occurrence was reported in 11 patients, metachronous in 19 patients (median time between the two diagnoses was 50 months, range 6-186, peak between 30–60 months). Gender and age (at the time of PDAC diagnosis) were noted in 21 of these 30 patients. There were 17 males and 4 females, median age 69 years (52–83).
In the metachronous group (19 cases), 7 patients were diagnosed with a focal form (6 head, 1 tail), 1 with a diffuse form, the information was not available in 11 patients. The location of PDAC was stated in 8 cases (3 in the pancreatic head, 3 in the body, 2 in the tail) and it arose in the part of the pancreas affected by AIP in only 3/8 (38%) patients (all head).
Patients with synchronous occurrence of conditions (11 cases) suffered from focal AIP in 6 cases (3 head, 2 body, 1 tail), diffuse type in 4 cases, the information was not available in 1 patient. PDAC was most often located in the head of the pancreas (4 cases), followed by the body and the tail (2 cases each). In one case PDAC affected the whole organ, the information was not available in 2 patients. Cancer occurred in the part of the pancreas affected by AIP in all (9/9) described cases.
**Conclusion:** There is a significant number of described cases of PDAC in patients with AIP in the literature. The majority of well described cases were metachronous with the tumor usually arising in the part of the pancreas affected by AIP. Although the risk of PDAC in AIP patients cannot be assessed by this review, the rather an unexpectedly high number of published cases should draw attention to a vigilant follow-up of patient with an established diagnosis of AIP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0108 KEY ENDOSCOPIC ULTRASOUND FINDINGS USEFUL FOR DIFFERENTIATING INVASIVE CARCINOMA FROM NON-INVASIVE HIGH-GRADE DYSPLASIA IN PANCREATOBILIARY TYPE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

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**Introduction:** Intraductal papillary mucinous neoplasm of the pancreas (IPMN) was classified into four histological subtypes: gastric, intestinal, pancreatobiliary (PB), and oncocytic. PB type IPMN is considered to have the most malignant potential and invasive carcinoma (IC) has poorer prognosis than noninvasive high-grade dysplasia (HD). It is therefore important to differentiate IC from HD. Endoscopic ultrasound (EUS) is more sensitive than other radiological methods for evaluation of intratumoral features of IPMN. In this study, we determined the key EUS findings that are useful for differentiating IC from HD in PB-type IPMN.
**Aims & Methods:** We retrospectively reviewed 124 patients with IPMN who underwent surgical resection between 2010 and 2015. Twenty-four cases were histologically classified as PB type. Two patients were excluded because of intermediate dysplasia. Twenty-two patients with PB-type IPMN, including IC ($n=11$) and HD ($n=11$), were enrolled in the present study. All patients underwent EUS before surgery. We retrospectively reviewed EUS findings to assess main pancreatic duct diameter, cyst diameter, mural nodule (MN) height, presence of ill-defined MN margin from the pancreatic parenchyma, and MN echogenicity.
**Results:** There were no significant differences in the clinical characteristics including gender and age between HD and IC. In HD/IC, the EUS findings were as follows. The number of main duct type, mixed type and branch duct type IPMN were 1/5, 4/2 and 6/4 cases, respectively. The mean diameter of the main pancreatic duct was $6.72 \pm 3.17/7.65 \pm 6.82$ mm. The mean diameter of the cyst, excluding main duct type, was $28.8 \pm 14.2/28.9 \pm 10$ mm. Definite MNs were seen in 9/11 cases. The mean height of the MNs was $20.6 \pm 9.7/10.9 \pm 9.06$ mm ($p=0.071$). Out of 9/11 definite MN cases, ill-defined MN margins from the pancreatic parenchyma were observed in 2/9 cases ($p=0.0077$). MNs with lower echogenicity than that of the pancreatic parenchyma were observed in 1/9 cases ($p=0.0017$). These two EUS findings about MNs were observed significantly more often in IC ($p=0.0010$).
**Conclusion:** In the PB-type IPMN, ill-defined MN margin from the pancreatic parenchyma and echogenicity of MN are the key EUS findings useful for distinguishing IC from HD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0109 ETHANOL VERSUS POVIDONE IODATE EUS-GUIDED FOR PANCREATIC CYSTIC LESIONS: A PROSPECTIVE AND COMPARATIVE STUDY

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**Introduction:** The EUS-guided ethanol lavage is a minimally invasive treatment modality in pancreatic cystic. The most common agents used are ethanol and paclitaxel, and rarely cause systemic effects1, 2. The literature has been reporting the use of povidone iodate for treatment of renal cysts and just one case in pancreatic cyst 3, 4.
**Aims & Methods:** This study evaluated the immediate occurrence of adverse events, the cyst size three months after the injection and the need for further lavage if the cyst does not shown reduction less than 30%. The inclusion criteria were no clinical condition or refuse to surgery, unilocular pancreatic cyst (1–8 cm). The patients were aleatory treated by EUS-guided with ethanol injection or povidone iodate, been the volume dependent of the cyst size. The technique used was puncture via a transduodenal or transgastric route and cystic fluid aspiration was performed using a curvilinear array echoendoscope and 19-Gauge needle. After subtotal evacuation of cystic fluid, injection of ethanol, which equals to that of aspiration, was performed.
**Results:** The ethanol injection was performed in 14 patients, with a mean injection of 27.6 ml (10–80 ml) and povidone iodate in 6 patients with a mean injection of 25.2 ml (2–50 ml). The cyst were serous adenoma (7.1%), pseudocyst (50%) and mucinous cyst (12.8) in the ethanol group and papillary mucinous neoplasm (33.3%), serous adenoma (33.3%) and pseudocyst (33.3%) in the iodine povidone group. The average size of the cysts in the ethanol group was 4.7 cm (2.5–7.8) and in povidone group was 4.5 cm (1.2–3.6). Average sessions for ethanol group was 1.4 (1–5) and povidone iodate was 1. The only adverse events found occurred in the ethanol group and it was pain (28.5%). The ablation cyst and decreased over 50% of the initial volume after ethanol and povidone was 14.2%, 83.3% [odds ratio (OR) = 3.75], 57.1% and 16.6% [odds ratio (OR) = 1.45], respectively.
**Conclusion:** The results of this study shows that the EUS-guided lavage with povidone iodate is a method as good as ethanol in the cystic ablation with a lower incidence of adverse events. Further prospective, randomized and comparative studies are need to confirm these benefits of povidone iodate in the conservative treatment of pancreatic cyst.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0110 NONINVASIVE NOVEL THERAPY OF HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) FOR UNRESECTABLE PANCREATIC CANCER

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**Introduction:** Recently, high-intensity focused ultrasound (HIFU) is most expected as new advanced therapy for unresectable pancreatic cancer (PC). HIFU therapy with chemotherapy is being promoted as new method to control local advance by ablation tumor, and mainly achieve relief of pain caused by PC.
**Aims & Methods:** We have evaluated the therapeutic effect of HIFU therapy in locally advanced and metastatic PC. We treated PC patients by HIFU as optional local therapy as well as systemic chemo / chemo-radiotherapy, with whom an agreement was obtained in adequate IC, from the end of 2008 in our hospital. This study took approval of member of ethic society of our hospital. HIFU device used is FEP-BY02 (Yuande Bio-Medical Engineering Co.LTD., China). The subjects were 120 PC patients, i.e. 62 cases in stage III, 58 cases in

stage IV. Performance status (PS) was PS:0; 74, PS:1; 44, and PS:2; 2 cases. Mean age was 61.7 ± 10.9 years, The details of therapy before HIFU treatment (overlap) was chemo-radiotherapy in 33, chemotherapy in 74, arterial infusion chemotherapy in 5, immunotherapy in 4, operation in 12, and BSC in 6 cases.
**Results:** All tumors were visualized by HIFU monitor system. Tumor location was head in 35, uncus in 19, body in 48, body ~ tail in 5, tail in 1, and others (recurrence) in 12 cases. Treatment data was followed; mean tumor size before and after therapy was 33.6 ± 10.3 and 33.6 ± 10.7 mm, mean treatment sessions: 2.4 ± 0.6 times, mean total treatment time: 111 ± 68.2 min, mean total number of irradiation: 2107 shots. The effects of HIFU therapy were the following; the rate of complete tumor ablation was 85.8%, the rate of symptom relief effect was 68.2%, the effectiveness of primary lesion was CR:0, PR:17, SD:76, PD:27 cases, primary disease control rate (DCR) more than SD was 77.5%. The therapy after HIFU treatment was operation in 8, chemotherapy in 100, immunotherapies in 3, and best supportive care (BSC) in 11 cases. MST after diagnosis in HIFU with chemotherapy and chemotherapy alone (38 patients in our hospital) was 997.8 vs 366.6 days, respectively ($p < 0.001$). MST after HIFU therapy was 582.7 days. Combination therapy of HIFU with chemotherapy was better result than common chemotherapy alone.
**Conclusion:** This study suggested that HIFU therapy has the potential of new method of combination therapy for PC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0111 SERIES OF 44 OPERATED PANCREATIC MUCINOUS CYSTIC LESIONS: CORRELATION BETWEEN MANAGEMENT RECOMENDATIONS (INTERNATIONAL, EUROPEAN AND AGA CONSENSUS) AND PATHOLOGICAL FINDINGS

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**Introduction:** Intraductal Papillary Mucinous Neoplasms of the pancreas are subcategorized clinically into Main Duct (MD-IPMN), Branch Duct (BD-IPMN) and Mixed Type (Mx-IPMN). MD-IPMN, Mx-IPMN and Mucinous Cystic Neoplasms (MCN) are considered lesions with malignant potential. Different International Consensus (IAP-2012, European-2013 and AGA-2015 guidelines) differ in criteria for surgical resection.
**Aims & Methods:** To analyze the suitability of a more conservative management regarding the predictive value of different risk criteria described for High Grade Displasia (HGD) or Invasive Carcinoma (IC). A retrospective multicenter study was performed, recruiting a total of 44 operated IPMN or MCN. Demographic, imaging, operative and pathological data, and outcomes were recorded.
**Results:** MD-IPMN: A total of 18 cases recruited, 89% male with a median age of 64 years old. 89% of them (16/18) showed HGD or IC in the post-surgery specimen analysis, and 81% (13/16) were symptomatic (PPV = 92.9%). One of the most frequent symptoms was jaundice (43.7% patients). And almost all symptomatic patients (except one) showed HGD or IC in the specimen analysis. Median size of lessions with any kind of malignancy (HGD or IC) was 36.7 mm (range: 15–80) while benign lesions (Low Grade Dysplasia) showed a median size of 27.5 mm (range: 20–35) ($p = 0.45$). All HGD or IC cyst presented at least one of the following criteria: size ≥ 30 mm (75%, PPV = 92.3%), Wirsung ≥ 5 mm (68.75%, PPV = 84.6), Worrisome features like intracystic mural nodules or thickened wall (68.75%, PPV = 100). BD-IPMN: A total of 10 cases recruited, 55.6% female, with a median age of 68 years old. 100% were symptomatic (probable selection bias, only operated lesions recruited) from which 50% (5/10) showed HGD or IC. Median size of lessions with any kind of malignancy was 43.8 mm (range: 22–70) while benign lessions showed a median size of 32.2 mm (range: 15–52, $p = 0.39$). Most cysts (80%) with HGD or IC presented at least one of the following criteria: Wirsung ≥ 5 mm, Worrisome features like intracystic mural nodulesor thickened wall (Sensitivity = 80%, Specificity = 100%). MCN: A total of 16 cases recruited, 87.5% female, with a median age of 50years old. 50% (8/16) were symptomatic and only 3/16 (18.75%) showed HGD or IC inthe pathologic analysis. All malignant lessions were symptomatic, with a median size of 103.7 mm (range: 35–200). Benign lessions showed a median-size of 43.7 mm (range 15–80, $p = 0.028$). Thus, size was an excellent predictor of benignity with a Negative Predictive Value for lessions under 40 mm of 85.7%, and 100% for lessions under 30 mm. No dilated Wirsung was observed and curiously, up to 30.7% of benign MCN presented orrisome features like mural nodules or peripheral calcifications (PPV = 33.3).
**Conclusion:** Our series supports the malignant rate described for MD-IPMN or BD-IPMN (88.9% vs 50%). Symptoms and morphological risk-criteria showed high specificity, but the size was not discriminant, supporting universal resection. MCN malignant rate was similar to that described in consensus (18.7%). Size was an effective discriminant factor (no malignancy in < 30 mm) supporting a more conservative management.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0112 PREDICTING FACTORS FOR UNRESECTABILITY IN PATIENTS WITH LOCALIZED PANCREATIC CANCER AND SELECTIVE USE OF STAGING LAPAROSCOPY

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**Introduction:** The prognosis for pancreatic cancer patients is very poor. At the time of pancreatic cancer diagnosis, only 15 ~ 20% of patients have a potentially resectable disease without evidence of a major vessel involvement or extrapancreatic spread of the tumor. Despite the advances and resolution improvement of imaging technologies, surgeons sometimes encounter distant metastasis intraoperatively, including liver metastases or small amount of peritoneal metastasis.
**Aims & Methods:** The aim of the present study was to identify the predicting factors for unresectability and to evaluate who should receive staging laparoscopy in patients with radiographically resectable pancreatic cancer. From 2006 to 2015, we retrospectively reviewed the medical records of 470 patients who diagnosed with pancreatic cancer and underwent open laparotomy at Severance Hospital, Seoul, South Korea. Information on age, sex, CA 19-9, total bilirubin, albumin, cholesterol, body mass index, tumor size, tumor location, and intraoperative finding were collected.
**Results:** Of the 470 patients who underwent open laparotomy, 32 (6.8%) patients were unresectability status on intraoperative finding and underwent open & closure or palliative bypass surgery. The tumor size and CA 19-9 in unresectable group were significantly larger than that in the resectable group. After matching by age and sex, multivariate analysis showed that tumor size was independent predicting factor for unresectability in radiographically resectable pancreatic cancer (hazard ratio, 1.214; 95% confidence interval, 0.473–0.994).
**Conclusion:** The presence of high-risk fators was associated with surgical unresectability in patients with radiographically resectable pancreatic cancer. The selective use of staging laparoscopy in patients high risk factors may decrease the frequency of unnecessary laparotomy in pancreatic cancer patient.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## MONDAY, OCTOBER 17, 2016 10:30–17:00

## ENDOSCOPY AND IMAGING I – POSTER EXHIBITION

### P0113 USEFULNESS OF AN E-LEARNING SYSTEM FOR THE ENDOSCOPIC DIAGNOSIS OF EARLY GASTRIC CANCER USING MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING: A RANDOMIZED CONTROLLED MULTICENTER STUDY

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**Introduction:** Magnifying endoscopy with narrow-band imaging (M-NBI), a recently developed image-enhanced endoscopic technique, can reportedly help distinguishing between cancerous and non-cancerous stomach lesions. For M-NBI diagnosis of early gastric cancer, the vessel plus surface classification system (VSCS) proposed by Yao et al [1] is very useful [2], and could require fewer biopsies to diagnose each cancer [3]. However, acquiring skill at M-NBI diagnosis takes substantial effort.

**Aims & Methods:** We have developed an internet-based e-learning system to teach diagnosis of early gastric cancer using M-NBI based on VSCS. This study was designed as a randomized controlled multicenter trial (UMIN: 000008569). We recruited endoscopists as participants from all over Japan. Initially, we conducted Test-1, which consisted only of M-NBI images of 40 gastric lesions (22 cancerous and 18 non-cancerous lesions) which were taken at maximum magnification. Participants were randomly assigned to the former-learning and the latter-learning groups. Pre-adjustment strata were their institutions, their numbers of endoscopies conducted, and their Test-1 scores. The former-learning group was allowed to access the e-learning system, which consisted of video lectures on the basics of M-NBI and VSCS, and self-exercise tests consisting only of M-NBI images of 100 gastric lesions to accumulate experience. We conducted Test-2 (same as Test-1) in both groups after the learning period. Following the Test-2, the same e-learning was given only to the latter-learning group before Test-3 (same as Test-1) was conducted for both groups. The analysis set of this study was the participants who scored $< 80\%$ accuracy on Test-1. The primary endpoint of this study was to compare the changes in diagnostic accuracy on Test-2 between groups. The secondary endpoint was to investigate the improvement of the diagnostic accuracies after e-learning in both groups.

**Results:** Among the 490 endoscopists from 77 institutions assessed for eligibility, 395 participants completed Test-1 and were enrolled; 198 were allocated to the former-learning group and 197 to the latter-learning group. The analysis sets of this study, excluding the 27 participants who scored $\geq 80\%$ on Test-1, were former-learning group: $n = 184$; and latter-learning group: $n = 184$. The former-learning group scored on average 59.9%, 67.3%, 67.4% in Test-1, Test-2, and Test-3, respectively, while the latter-learning group's average scores were 61.7%, 61.8%, 68.4%, respectively. The mean change in accuracy on Test-2 was significantly higher in the former-learning group than in the latter-learning group ($7.4 \pm 8.6\%$ and $0.14 \pm 7.5\%$, $P < 0.001$), when e-learning was given only to the former-learning group. After e-learning in both groups, the mean accuracy on Test-3 in the latter-learning group improved even to that in the former-learning group ($P = 0.323$).

**Conclusion:** This study clearly demonstrated the efficacy of the e-learning system. Endoscopists can take advantage of this e-learning system at any one time to learn gastric M-NBI diagnosis using VSCS and improve their capabilities to differentiate and diagnose cancer and non-cancer using M-NBI.

Diagnostic accuracy in each tests

| | Former-learning group n = 184 | Latter-learning group n = 184 |
|---|---|---|
| Test-1, %, mean ± SD | 59.9 ± 8.2 | 61.7 ± 8.6 |
| Test-2, %, mean ± SD | 67.3 ± 8.6 | 61.8 ± 10.2 |
| Test-3, %, mean ± SD | 67.4 ± 8.5 | 68.4 ± 9.2 |

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0114 RANDOMIZED CONTROLLED TRIAL (RCT) OF DOPPLER ENDOSCOPIC PROBE (DEP) ASSISTED TREATMENT COMPARED TO STANDARD HEMOSTASIS OF SEVERE VARICEAL OR PORTAL HYPERTENSIVE LESION UGI BLEEDING

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**Introduction:** Visually guided endoscopic treatment of variceal bleeding is the current standard of care. Residual blood flow in varices causes rebleeding but is not currently used for hemostasis.

**Aims & Methods:** In a RCT, our primary outcome was 30 day lesion rebleed rates of patients treated either with standard endoscopic hemostasis or DEP guided therapy. Secondary outcomes were complications, surgeries, TIPS, death, transfusions, & hospital days. Cirrhotics were resuscitated, screened, & consented before endoscopy – EGD (if they met clinical entry criteria) & had severe UGI bleeding (clinical signs, hemoglobin drop of $>2$ gms, & RBC transfusions). Randomization was during EGD for esophageal varices-EV's (with or without stigmata of hemorrhage – SRH –active bleed, platelet plug, clot, spot); gastric varices (GVs), post-rubber band ligation (RBL) ulcers, or Mallory Weiss tears (MWT) with SRH. Patients had airways protected, antibiotics & Octreotide (OCT) infusions, & RBL hemostasis (distally & on SRH & for varices or MWT- minimum 2 bands/column). Sclerotherapy was used to control severe active bleeding first; for GVs & post-RBL ulcers; & during FU for varices too small to band. For DEP patients, varices & other lesions were interrogated near SRH & distally & again after hemostasis using DEP depth settings $<4$ mm with disposable probes & FDA approved Doppler unit (Vascular Technology Inc, Nashua, NH). For residual lesion blood flow by DEP after standard treatment, more RBL &/or sclerotherapy was applied to obliterate flow, if deemed safe by endoscopists. All patients received OCT infusions (50 micrograms/hr) for 72 hours & twice daily PPIs & were managed in ICUs by physicians & nurses blinded to whether DEP was used. EGD was repeated for severe UGI rebleeding or varix surveillance in 7–14 & 30 days. For continued bleeding TIPS was performed. Research coordinators followed patients prospectively, data management was with SAS, & $p < 0.05$ was considered statistically significant.

**Results:** For 87 RCT patients, 79% had EVs & 21% other lesions. No differences were significant in lesions or baseline clinical variables for the 2 treatments. A significant difference (21.2% higher) was in 30 day rebleed rate for Standard vs. DEP patients (17/47 vs. 6/40 – $p = 0.0302$) – Odds ratio 3.21 (95%CIs 1.12, 9.2); Number Needed to Treat was 4.7. 30 day rates of surgery (OLT – 3 vs. 1), TIPS (3 vs. 4), or deaths (2 vs. 1) were not significantly different but RBC & FFP transfusions & hospital days were. No major complications occurred.

**Conclusion:** Cirrhotics with bleeding varices, post-RBL ulcers, or MWTs treated with DEP guided hemostasis had significantly lower 30 day rebleed rates, RBC or FFP transfusions, & hospital days than those treated with standard visually directed treatment without blood flow monitoring. 2. DEP was fast, safe, & easy to use. Supported by a Clinical Veterans Administration Merit Review Grant (CLIN-013-07F) and NIH NIDDK 41301 CURE DDRC Human Studies Core. Registered on ClinTrials.gov (NCT00732212).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0115 RESULTS OF ENDOSCOPIC EN-BLOC RESECTION OF SUB EPITHELIAL TUMORS: A SINGLE CENTRE STUDY

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**Introduction:** Sub epithelial tumors (SET's) are soft tissue tumors arising from the submucosal or muscluaris propria layers of luminal organs. Enbloc resection of these lesions is desirable; often using surgical methods. Endoscopic techniques for resection of these lesions include endoscopic submucosal dissection (ESD) for lesions originating in the sub mucosal layer or endoscopic full thickness resection (EFTR) or submucosaltunneling endoscopic resection (STER) for lesions arising in the muscularis propria layer. This study describes ourexperience of endoscopic treatment of SETs.

**Aims & Methods:** Data of all consecutive patients undergoing endoscopic resection of SET in the period 2012 –2015 was analyzed. All patients underwent pre procedure screening esophagogastroduodenoscopy (EGD) andendoscopic ultrasound (EUS) for assessment of SET and layer of origin. One of following 3 procedures – ESD, EFTR or STER was performed for resection of the SET. ESD was performed for SETs arising in sub mucosal layer whereas EFTR or STER was performed for lesions in the muscularis propria layer. All patients underwent follow up EGD at 4–6 weeks. Parameters recorded were – location of lesion, layer of origin, procedure performed (ESD, EFTR or STER), technical success, closure techniques, margin positivity on histology, complications and their management and final histopathology.
**Results:** 34 consecutive patients with sub epithelial tumors underwent endoscopic resection during study period. Mean age – 57 years (range 29–78) and 24 male patients. ESD was performed in 25 patients, EFTR in 7 and STER in 2. Endoscopic closure was performed whenever deep muscle layer was breached. Full-thickness clip was applied in 2, mucosal clip (hemoclip) with omental patch closure in 1, hemoclip approximation of full-thickness defect in 1 and hemoclip approximation of muscle defect in 12 patients. Mucosal incisions after STER were closed using hemoclips in 2 patients. Location of SETs was stomach (15), colon (6), duodenum (9), esophagus (3) and rectum (1). The mean area of sub epithelial tumors was 11.26 $cm^2$ (range 1–110). Histology was neuroendocrine tumors – 12, lipoma – 7, gastrointestinal stromal tumors – 8, leiomyoma – 5, ectopic pancreatic rest – 1 and duplication cyst – 1. Technical success of resection was 100%. 3 complications: perforation – 2 patients, 1 required surgery; bleeding – 1 patient, managed endoscopically. Histopathology of all specimens showed en-bloc excision with negative tumor margins.
**Conclusion:** Conclusions: Endoscopic en-bloc resection using ESD, EFTR or STER is a safe and effective therapy for SETs. Pre procedure EUS can determine the appropriate excision procedure to be performed. Endoscopic closure using mucosal or full-thickness clips is safe and effective.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0116 ASSESSMENT OF THE SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN VERY ELDERLY PATIENTS

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**Introduction:** Since endoscopic submucosal dissection (ESD) has been developed for en bloc resection of large superficial tumors, it is widely accepted as a reliable therapeutic procedure. This recent innovation allows safe treatment in elderly patients; however, there are only few reports of ESD in very elderly patients, aged 80–90 years old or above. This study aimed to assess the safety and feasibility of ESD in the very elderly patients.
**Aims & Methods:** Between June 2013 and March 2016, patients with superficial gastrointestinal lesions at our institution were treated with ESD. A standard gastroscope (GIF-Q 260Z, Olympus) and a Dual knife (KD-650Q, Olympus) were used for ESD. All patients were treated under conscious sedation with midazolam (1–10 mg). Patients were divided to an elderly group (60–79 years of age) and a very elderly group (above 80 years of age). For both groups, lesion size, procedure time, total amounts of midazolam, and ESD-related complications (hypotension, hypertension, hypoxia, arrhythmia, and bleeding) were analyzed.
**Results:** From the database, we collected data on a total of 293 patients who underwent ESD for esophageal (39 cases), gastric (123 cases), and colorectal lesions (131 cases) more than 60 years old in our institution. In the elderly group, 161 patients were treated (89 males/ 72 females, 60–79 years of age, mean age 73.1) and in the very elderly group, 133 patients were treated (68 males / 64 females, 80–92 years of age, mean age 84.7). All patients were successfully treated with ESD in both groups. The mean resected specimen size was 34.4 mm in the elderly group and 34.3 mm in the very elderly group ($p = 0.98$). ESD time was 61.5 minutes in the elderly group and 56.1 minutes in the very elderly group ($p = 0.32$). Midazolam doses of 3.8 mg and 3.6 mg were administered ($p = 0.38$), respectively. As complications, hypoxia were 32.2% and 51.9% ($p < 0.05$), bradycardia were 12.4% and 18.0% ($p = 0.17$), tachycardia were 11.8% and 12.0% ($p = 0.45$), hypotension were 68.9% and 66.2% ($p = 0.67$), hypertension were 30.4% and 29.3% ($p = 0.86$), respectively. Based on the final pathological results, there were 2 cases on whom additional gastrectomy was performed, and 1 case of radiation in the elderly group; and no additional therapy was performed in the very elderly group.
**Conclusion:** Our data suggests that ESD is safe and feasible in very elderly patients; however, such patients tended to be more sensitive to sedation. Our data also suggests that general anesthesia might not be necessary for the elderly and very elderly patients undergoing ESD, as long as there is appropriate intraoperative management. Further investigations to evaluate various other factors including past medical history, performance status, and anticoagulant medicine are necessary.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0117 DIAGNOSTIC YIELD OF ENDOSCOPIC ULTRASONOGRAPHY (EUS) FOR SUBMUCOSAL INVASION OF SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC), A POST HOC ANALYSIS OF MULTICENTER PROSPECTIVE CONFIRMATORY STUDY (JCOG0508)

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**Introduction:** Accurate diagnosis of submucosal (SM) invasion of esophageal squamous cell carcinoma (ESCC) is difficult by conventional endoscopic examination, especially in case of slight or moderate SM invasion. Endoscopic ultrasonography (EUS) has been used for evaluation of the depth of cancer invasion worldwide[1–3], however, there is no prospective, multicenter study to evaluate the diagnostic yield of EUS for ESCC.

Correlation between clinical and pathological depth of invasion.

| | Pathological diagnosis | | | | | |
|---|---|---|---|---|---|---|
| Clinical diagnosis | pEP | pLPM | pMM | pSM1 | pSM2 | total |
| cSM1 | 3 | 28 | 44 | 14 | 25 | 114 |
| cSM2 | 0 | 3 | 11 | 3 | 44 | 61 |
| total | 3 | 31 | 55 | 17 | 69 | 175 |

**Aims & Methods:** The aim of this study is to evaluate endoscopic diagnostic yield of EUS for SM invasion as a post hoc analysis using the data of multicenter prospective study as well as to explore clinical features that influenced the clinical diagnosis. JCOG0508 was a multicenter prospective confirmatory study to evaluate the efficacy and safety of combined treatment of endoscopic resection (ER) and chemoradiotherapy for clinical (c) Stage I (cSM-slight or moderate) ESCC [4]. All lesions were evaluated with both conventional endoscopy and EUS before enrollment. If the differential diagnosis between cT1a-musclaris mucosa (MM) and cT1b-SM-slight was difficult, it was judged as cT1b-SM-slight. We compared the clinical and pathological (p) diagnosis for depth of invasion and assessed the diagnostic yield: positive predictive value (PPV) for SM (pSM/cSM), PPV for the patient diagnosed with cSM but pMM or pSM (pMM + pSM/cSM). We also investigated what factors affected the pathological depth of invasion. The factors included macroscopic type, tumor size, circumference of the lesion, and clinical evaluation of depth of invasion (cSM-slight vs cSM-moderate).
**Results:** Of 177 patients enrolled in JCOG0508, two patients were excluded because of withdrawal of consent and invasion depth of pMM with unknown vertical margin. Finally, 175 patients were analyzed. The numbers of the macroscopic type with 0-I/ 0-IIa/ 0-IIb/ 0-IIc were 18/ 30/ 4/ 123, respectively. The median size of lesion was 2.5 cm (range: 0.5–5.0). The circumference of the lesion in the esophageal lumen; $<1/2$/ $>1/2$ and $<3/4$ were 152/ 23. The number of patients with cSM-slight and cSM-moderate were 114 and 61, respectively. The number of patients with pEP/ pLPM/ pMM/ pSM1/ pSM2 were 3/ 31/ 55/ 17/ 69, respectively. The PPV for SM was 49.1% (86/175) and PPV for the patient diagnosed with cSM but pMM or pSM was 80.6% (141/175). A multivariate analysis demonstrated that clinical evaluation (cSM-slight vs cSM-moderate) was an independent factor associated with the discrimination of pM from pSM (OR 6.65, 95%CI 3.21–13.75).
**Conclusion:** The PPV of endoscopic diagnosis for submucosal invasion of ESCC was not high enough even with EUS. Especially, clinically diagnosed SM-slight ESCC is likely to be pathological mucosal cancer. Such lesions could be curatively treated by ER alone. Therefore, ER could be recommended for these lesions as an appropriate diagnostic procedure as an initial part of minimally invasive treatment strategy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0119 MODIFIED PERORAL ENDOSCOPIC SHORTER MYOTOMY FOR THE TREATMENT OF SIGMOID-TYPE ACHALASIA: A PILOT STUDY


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**Introduction:** Peroral endoscopic myotomy is a promising minimally invasive treatment for achalasia. It is also reported that this new therapy was effective for treating achalasia with sigmoid esophagus.
**Aims & Methods:** The aim of the study was to examine the feasibility and safety of a novel modified peroral endoscopic shorter myotomy for sigmoid-type achalasia. Between July 2011 and August 2015, 11 achalasia patients (6 male, with a mean age of 41 years) with sigmoid esophagus underwent peroral endoscopic shorter myotomy in our department. Diagnosis was based on symptoms, manometry, radiology and endoscopy. Preoperative and postoperative symptoms scores, manometry outcomes and quality of life scoring of achalasia were recorded and analyzed.
**Results:** All patients had dysphagia as their chief presenting complaint with the median duration of 21 months (range 18–36 months). Procedure was performed successfully in all patients, and the mean time required for the procedure was 56.8 minutes (range 49–70 minutes). There were no mortalities and major postoperative complications occurred. The mean length of myotomy was 5.2 cm (range 5–6 cm). During a mean follow-up period of 23 months (range 12–37.5 months), treatment success (Eckardt score $\leq 3$) was achieved in all patients. There was a significant improvement of symptoms relief, lower esophageal sphincter pressure decrease and quality of life ($P < 0.01$, $P < 0.01$, $P < 0.01$, respectively). Symptoms of gastroesophageal reflux occurred in two patient, and it was easily controlled with regular doses of proton pump inhibitors.
**Conclusion:** In this study, peroral endoscopic shorter myotomy is feasible, effective and safe in improving subjective, objective, and quality-of-life outcome measures in patients with sigmoid-type achalasia. Further studies are warranted to prove its long-term efficacy in comparison to other treatment modalities.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0120 EFFICACY, RECURRENCE AND COMPLICATION RATES OF ENDOSCOPIC MUCOSAL RESECTION VERSUS ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY BARRETTÍS NEOPLASIA: A RETROSPECTIVE GERMAN SINGLE CENTER ANALYSIS


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**Introduction:** Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are established standard treatment options for superficial Barrett's neoplasia. Whereas EMR is the most comprehensively studied method with the advantages of being effective and safe, ESD has potential advantages regarding a high en bloc resection rate and better histopathologic assessment for accurate staging, but it is technically more demanding and may cause more adverse events. So far, there are only few data comparing both endoscopic techniques for treatment of early Barrett's neoplasia in a long-term follow-up.
**Aims & Methods:** We aimed to assess EMR compared to ESD in terms of curative resection rates, complication and recurrence rates. In the retrospective single center analysis, all patients were included in which an EMR ($n = 56$) or ESD ($n = 53$) was performed between 2003 and 2015 due to a visible suspicious Barrett's lesion or a histologically confirmed Barrett's associated high-grade intraepithelial neoplasia (HGIN) or an early Barrett's carcinoma (BC). EMR was carried out in form of one or by serial endoscopic resections while ESD was performed in one session.
**Results:** In 39 of 56 patients who underwent EMR, histological assessment showed HGIN ($n = 8$) or BC ($n = 31$). 49 of 53 patients treated with ESD showed HGIEN ($n = 5$) or BC ($n = 44$). Specimen histology revealed no neoplasia in 17 and 4 patients, respectively, despite of visible suspicious Barrett's lesion or previous biopsy-proven HGIN. R0 resection defined as margins free of HGIN and BC was achieved in 76.9% (30/39) by EMR and in 81.6% (40/49) by ESD ($p = 0.6057$). Regarding a subgroup which showed an invasion less than pT1sm2, R0 resection was observed in 77.8% (28/36) and 97.3 (36/37), respectively ($p < 0.05$). After R1 resection, surgical or endoscopic resection ± ablative therapy was carried out according to the histological tumor category. EMR and ESD did not lead to complications requiring surgery. Furthermore, there were no significant differences in the risk of delayed bleeding, perforation and stricture rates when comparing EMR to ESD. Delayed major bleedings were observed in 3.6% (2/56) after EMR and 3.8% (2/53) after ESD, periinterventional perforations occurred in 1.8% (1/56) and 7.5% (4/53), respectively ($p = 0.1976$). Esophageal strictures developed in 25.0% (14/56) after EMR, partially due to serial endoscopic resections and in 18.9% (10/53) after ESD ($p = 0.4936$), all treated endoscopically. After EMR, recurrent BC was observed in 10.3% (4/39, mean endoscopic follow-up 61 ± 46 months), thereof three patients with initially mucosal and one with submucosal invasion. After ESD, recurrent BC was observed in 6.1% (3/49, mean endoscopic follow-up 26 ± 20 months), thereof one patient with initially mucosal and two with submucosal invasion ($p = 0.4578$).
**Conclusion:** EMR and ESD are both highly effective endoscopic resection options in early Barrett's neoplasia. In the analysed cohort, ESD achieves higher R0 resection rates than EMR in tumors with mucosal and superficial submucosal invasion, but not in lesions which show an invasion greater than pT1sm1. Both techniques are associated with low recurrence rates without significant differences. ESD is not associated with higher complication rates than EMR.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0121 ENDOSCOPIC HAND SUTURING FOR MUCOSAL DEFECT CLOSURE AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION IN IN VIVO ANIMAL MODELS AND CLINICAL CASES


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**Introduction:** Mucosal defect closure after gastric endoscopic submucosal dissection (ESD) may prevent postoperative bleeding and delayed perforation. Although several clipping techniques have been introduced, endoclips are too weak to maintain closure and may be too small for large mucosal defect closure after ESD. Endoscopic hand suturing (EHS) was developed to provide more reliable closure without a size limitation)[1].
**Aims & Methods:** In this pilot study, we aimed to demonstrate the feasibility of EHS and possibility of permanent closure after gastric ESD in in vivo animal models and clinical cases. [Animal experiment] The institutional review board of our animal laboratory approved the study; EHS was performed in 6 live pigs. A mucosal defect (3 cm in size) was made in each pig. The mucosal layers were continuously sutured in a linear fashion using a prototype of a through-the-scope needle holder (Olympus) and an absorbable barbed suture (V-loc180; Covidien) with a haemoclip or a knot on the tail as an anchor. After suturing, the remaining part of the needle and thread was cut with scissor forceps and was retrieved transorally. Suturing sites were endoscopically observed at most on the 7th day following the procedure. The success rate of EHS and suture maintenance were investigated. [Clinical study] The institutional review board of our hospital approved the study; EHS was performed in 8 patients who underwent ESD for gastric neoplasms (3 cm or less in size) using the above-mentioned procedure. The patients were endoscopically monitored at postoperative week 1 and 4. The success rate of EHS and maintenance of the suturing were assessed, including postoperative adverse events.
**Results:** [Animal experiment] In the all 6 pigs, EHS was successfully completed (100%). However, the sutured sites collapsed in the first 3 cases on the 7th day following the procedure. In the latter 3 pigs, the sutures were reinforced with additional clipping and closely monitored endoscopically on every 2 days after the procedure; however, these also reopened in all cases on the 4th day following the procedure. [Clinical study] EHS was completed in all 8 cases (100%), and no severe adverse events occurred during the procedure and thereafter. The median diameter of the mucosal defect, procedure time and the number of stitches were 32 mm (range, 20–37 mm), 20 min (range, 13–18 min) and 7 (range, 6–10), respectively. In the first 4 cases, the sutures collapsed at postoperative week 1. Therefore, we attempted to insert the needle deeply in the horizontal direction and to pull the strings more tightly in the latter 4 cases. Consequently, sutures were successfully maintained at 1 and 4 weeks following the procedure in these cases.
**Conclusion:** EHS was feasible in both in vivo animal models and human cases, and the closure was maintained by suturing the mucosal defects deeply and tightly in clinical cases. EHS, which enables optimally designed intraluminal suturing by peroral flexible endoscopy, appears to be helpful in avoiding postoperative adverse events after gastric ESD and therefore in shortening the hospitalization period (UMIN000017125).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0122 IMPROVED VISIBILITY OF EARLY GASTRIC CANCER USING IMAGE-ENHANCED LASER ENDOSCOPY

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**Introduction:** Endoscopic examination is essential for diagnosis of gastric cancer and atrophic gastritis. Blue laser imaging (BLI) including a brighter BLI-bright was developed as a novel image-enhanced laser endoscopy for a narrow-band light observation. Moreover, linked color imaging (LCI) was developed to recognize slight differences in mucosal color for detection of tumor and mucosal inflammation. It is unknown which is better visibility for diagnosis of early gastric cancer (EGC) and atrophic gastritis among white light imaging (WLI), BLI (BLI-bright), LCI and flexible spectral imaging color enhancement (FICE).
**Aims & Methods:** We investigated which is better visibility for diagnosis of EGC and atrophic gastritis among white light imaging (WLI), BLI (BLI-bright), LCI and flexible spectral imaging color enhancement (FICE). We recorded non-magnifying and magnifying observation videos of consecutive 40 cases with EGCs by using WLI, BLI (BLI-bright), LCI and FICE. Five endoscopists evaluated the videos in a randomized order. The visibility of EGC and atrophic border was assigned a visibility score from 4 (excellent) to 1 (poor). The visibility scores in each mode and their relationship to EGC and atrophic border were analyzed. Atrophic border was evaluated by Kimura-Takemoto classification. This study was approved by the Ethical Review Committee of the Kyoto Prefectural University of Medicine and carried out in accordance with the Helsinki Declaration of the World Medical Association.
**Results:** Six EGCs were located in upper third of stomach, 20 were in middle third, and 14 were in lower third. There were 32 well-differentiated adenocarcinoma, three moderately differentiated adenocarcinoma, and five poorly differentiated adenocarcinoma. There were six cases with mild atrophy (C-1 and C-2), 12 cases with moderate atrophy (C-3 and O-1), 22 cases with severe atrophy (O-2 and O-3). The mean tumor size was 12 mm (9–40). The mean visibility scores of BLI-bright and LCI for EGC in a distant observation were significantly higher than those of WLI and FICE (3.51, 3.34, 3.04, and 3.14; $P = 0.002$, respectively). The mean visibility scores of BLI for EGC in a magnifying observation were significantly higher than those of WLI, LCI, and FICE (3.81, 2.61, 3.28, and 3.07; $P < 0.0001$, respectively). The mean visibility scores of LCI for atrophic border in a distant observation were significantly higher than those for WLI, BLI-bright, and FICE (2.78, 2.73, 2.24, and 2.52; $P = 0.001$, respectively).
**Conclusion:** EGCs were more visible in a distant observation by using BLI-bright or LCI compared with WLI and FICE. EGCs were more visible in magnifying observation by using BLI compared with WLI, LCI, and FICE. Atrophic border was more visible by using LCI compared with WLI, BLI-bright, and FICE. Therefore, LCI was the most suitable for detection of EGC and atrophic gastritis. On the other hand, BLI was the most suitable for detailed magnifying observation of EGC.
**Disclosure of Interest:** Y. Itoh: Y. Itoh was affiliated with a department that was partially funded by Fujifilm Medical Co., Ltd. (J082003006).
All other authors have declared no conflicts of interest.

## P0123 EFFECT OF ANTICOAGULANTS ON THE RISK OF DELAYED BLEEDING AFTER GASTRIC ESD

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**Introduction:** Anticoagulants are used to reduce the risk of thromboembolic events and increasing evidence support them to prevail. direct oral anticoagulants (DOAC) are our new choice, however, there is no report about the effect to endoscopic treatments.
**Aims & Methods:** This is a retrospective study of three referral institutes. We treated with ESD gastric neoplasm in 97 patients who were taking anticoagulants. We divided the patients into the two groups, warfarin group and DOAC group. We researched patients' background, treatment results, complication, and hospitalization period.
**Results:** Seventy-three patients were taking warfarin and 24 patients were taking DOAC including 12 patients on dabigatran, 11 patients on rivaroxavan, 1 patient on apixavan. In warfarin group, 78% of patients were performed heparin replacement (HR) as a bridge therapy for perioperative cessation period and delayed bleeding rate was significantly higher in patients with HR than in patients without HR (36% vs 0%, $p < 0.05$). In DOAC group delayed bleeding rate was significantly higher in patients with rivaroxavan than in patients with dabigatran (45% vs 0%, $p < 0.05$), with no relation to HR. As the number of taking antithrombotic agents increased, delayed bleeding rate became higher. Compared to warfarin, period of HR was required shorter ($p < 0.05$) in DOAC, because DOAC reach to maximum effect shortly, and hospitalization period were also shorter ($p < 0.05$). Multivariate analysis showed HR (OR 10.7), rivaroxaban (OR 6.00), and multiple antithrombotic agents (OR 4.35) were independent risk factors of delayed bleeding. Thrombotic event (cerebral infarction) was developed in one patient, who discontinued warfarin with HR.
**Conclusion:** Dabigatran was attractive alternative for warfarin to reduce the period of hospitalization and delayed bleeding rate, although rivaroxaban had significantly higher risk of delayed bleeding. The effect of DOAC differs in each agents.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0124 DETECTION OF UPPER GASTROINTESTINAL BLEEDING WITH A NOVEL TELEMETRIC SENSOR CAPSULE (HEMOPILL ACUTE) – A PROSPECTIVE PILOT STUDY

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**Introduction:** Due to the lack of reliable non-invasive methods to detect upper gastrointestinal bleeding (UGIB), decision on timepoint of endoscopy is usually based on clinical parameters as well as on local resources and expertise. In preclinical trials, a novel telemetric swallowable photometric sensor capsule was able to reliably detect blood in the upper GI tract.
**Aims & Methods:** The aim of this pilot study was 1) to evaluate saftey of the device and 2) to determine parameters and threshold levels of the measurement signals in a clinical real-life Setting. We conducted a prospective non-randomized cohort study at a tertiary referral center. Patients with symptoms of UGIB without evidence of hemorrhagic shock swallowed the sensor capsule immediately after presentation in the emergency department. The capsule is battery-powered and contains an optical sensor and a telemetry unit that sends measurement values in real time to an extra-corporal reciever. Independet of the measurement values, all patients recieved esphagogastroduodenoscopy (EGD) within 12 hours.
**Results:** From April 2015 to Febuary 2016, 30 patients were included in the study. Ingestion of the capsule was feasible and without adverse events in all patients. EGD showed active bleeding in 3 patients and signs of recent bleeding in 10 patients. We chose the maximal quotient (Q) of the measurement values generated within the first ten minutes after capsule ingestion as parameter for detection of blood. A threshold level of $Q = 40$ or $Q = 10$ (depending on timepoint of last meal) was defined. Using this parameter, the capsule was able to correctly detect UGIB in 12 patients. In one case, bleeding was probably generated during EGD and therefore not detected by the sensor. The correlation coefficent (Kendall Tau) was 0.727 ($p < 0.0001$). All 15 patients without endoscopic evidence of UGIB were correctly recognized as negative by the capsule. We observed one case of aspiration of gastric content during EGD, there were no adverse events related to the capsule. Capsule excretion could be documented in 25 patients, there was no evidence of capsule retention.
**Conclusion:** Non-invasive detection of UGIB with the novel telemetric sensor capsule is feasible and safe. The measurement values generated within the first ten minutes after ingestion correlated significantly with the presence or absence of UGIB. Prospective multicenter studys are required to confirm the results of this pilot study.
**Disclosure of Interest:** A. Schmidt: Dr. Schmidt has recieved lecture fees from Ovesco Endoscopy.
K. Caca: Prof. Caca has recieved lecture fees from Ovesco Endoscopy.
All other authors have declared no conflicts of interest.

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## P0125 OVER-THE-SCOPE CLIP SYSTEM VERSUS ENDOLOOP COMBINED WITH METAL CLIPS APPLIED TO CLOSURE OF PERFORATION IN GASTRIC ENDOSCOPIC FULL-THICKNESS RESECTION: A SINGLE-CENTER PROSPECTIVE COMPARISON STUDY

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**Introduction:** Endoscopic full-thickness resection (EFTR) is a novel endoscopic resection method based on the developed techniques of endoscopic submucosal dissection (ESD) and endoscopic submucosal excavation (ESE). EFTR without laparoscopic assistance has been deemed to be an efficacious, safe, and minimally invasive therapeutic method for the treatment of gastric submucosal tumors (SMTs). The technique makes it possible to resect deep upper gastrointestinal (GI) lesion and provide complete specimen for acquiring precise pathological diagnosis. Since EFTR leads to artificial perforation, the key stage of the

procedure is successful closure of the wall defect after resection, to prevent peritonitis and the need for surgical intervention. The use of endoloop combined with metal clips is still a widely accepted closure technique, but it is time-consuming, and the effectiveness of it is more dependent on the operators' skill. Over-the-scope clip (OTSC) system, as a novel closure technique, seems to be time-saving and make closure much easier to perform.
**Aims & Methods:** The study aimed to compare safety and efficacy of a novel closure device, OTSC system, with endoloop and metal clips, applied to gastric EFTR for SMTs. A prospective study was carried out, including a consecutive cohort of 40 patients who underwent EFTR for gastric SMTs between March 2014 and June 2014 in our center. According to the different closure methods applied to perforation resulting from EFTR, the patients were divided into two groups, OTSC group (n = 20) and endoloop and metal clips group (n = 20). The demographic and operation-related parameters of the two groups were compared used statistical approach by statistical software SPSS 20.
**Results:** EFTR and closure procedure were both performed successfully in all of the patients. R0 resection was achieved in every patient. The data, including clinicopathological characteristics of the patients and comparison of the parameters between the OTSC group and endoloop and metal clips group, is listed in Table 1. There was no significant difference in patient age, sex, tumor size and perforation size between the two groups. The operation time, closure time, total complication rate and hospital stays in OTSC group were all shorter than those in endoloop and metal clips group, but it showed no statistical difference between the two groups. The operation cost in OTSC group was significantly less than that in endoloop and metal clips group. Clip retaining rate in OTSC group was significantly higher than that in endoloop and metal clips group. There were two and four cases occurred seroperitoneum or pleural effusion in OTSC group and endoloop and metal clips group, respectively. All those complications disappeared spontaneously. Delayed bleeding and perforation were detected in one case in endoloop and metal clips group, and the patient suffered secondary surgery to stop bleeding and repair perforation. No other severe complications developed in the two groups. During the follow-up ranged from 17 to 19 months, all OTSC were proved to stay in situ by gastroscopy. No procedure-related death occurred in the study.

**Table 1:** Clinicopathological characteristics of the patients and comparison of the parameters between the over-the-scope clip (OTSC) group and endoloop and metal clips group.

| | OTSC group (n = 19) | Endoloop and metal clips group (n = 21) | P-value |
|---|---|---|---|
| Age, years, mean ± SD | 58.7 ± 14.2 | 61.8 ± 9.9 | 0.421 |
| Sex, male/female | 8/11 | 14/7 | 0.119 |
| Tumor location: GB/GF/GA | 7/9/3 | 9/9/3 | |
| Tumor size, mm, mean ± SD | 2.5 ± 0.6 | 2.0 ± 0.9 | 0.056 |
| Perforation size, mm, mean ± SD | 2.3 ± 0.6 | 1.9 ± 0.9 | 0.086 |
| Procedure time, min, mean ± SD | 45.9 ± 10.6 | 56.6 ± 41.9 | 0.286 |
| Closure time, min, mean ± SD | 14.2 ± 2.8 | 15.7 ± 9.5 | 0.508 |
| R0 resection (%) | 100 (19/19) | 100 (21/21) | |
| Success Closure procedure (%) | 100 (19/19) | 100 (21/21) | |
| Complications (%) | | | 1.000 |
| Seroperitoneum (%) | 5.3 (1/19) | 9.5 (2/21) | |
| Pleural effusion (%) | 0 | 4.8 (1/21) | |
| Delayed perforation (%) | 0 | 4.8 (1/21) | |
| Delayed bleeding (%) | 0 | 4.8 (1/21) | |
| Convertion to surgery (%) | 0 | 4.8 (1/21) | |
| Mean hospital stays, day, mean ± SD | 3.8 ± 1.2 | 5.3 ± 3.4 | 0.078 |
| Operation cost, thousand yuan, mean ± SD | 18.7 ± 0.7 | 1.9 ± 0.1 | 0.000 |
| Clip retaining rate | 89.5 (17/19) | 14.3 (3/21) | 0.000 |

**Conclusion:** The two closure methods, OTSC and endoloop combined with metal clips, both appeared to be feasible, safe and effective for repairing gastric perforations. Compared with endoloop and metal clips method, OTSC was easier to operate, more efficient and might require shorter operation time. However, OTSC required higher cost, and its rate of clip retention in the body was much higher than that of endoloop and metal clips.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0126 TWO DIFFERENT ENDOSCOPIC LONG INTESTINAL TUBE PLACEMENTS FOR SMALL BOWEL OBSTRUCTION: TRANSNASAL ULTRATHIN ENDOSCOPY VERSUS CONVENTIONAL ENDOSCOPY

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**Introduction:** Small bowel obstruction (SBO) is a common problem in general surgery and is associated with considerable morbidity and mortality. It is commonly caused by postoperative adhesions, and sometimes by the recurrence and metastasis of the abdominal tumor. The conventional method is to intubate a common nasogastric tube, which can only suction the fluid in the stomach, and has limited effects. In recent years, the long intestinal tube has been applied for intestinal decompression and proved to be efficient and necessary for the treatment of patients who suffer the SBO, especially those with partial obstruction. The early studies reported that most long intestinal tubes are inserted only under fluoroscopy which had some disadvantages such as the long operation time and the exposure to more radiation. As the endoscopic technique develops, more investigators have tried endoscope-guide intubation to facilitate the procedure. A novel endoscopy with a transnasal ultrathin endoscopy was shown to be more convenient and better tolerated by patients. However, although there are some researches reporting the advantages of placing the long intestinal tube with the help of transnasal ultrathin endoscope over placing the tube under fluoroscopy, few investigators have compared the effects of transnasal ultrathin endoscopy and conventional endoscopy for placement of a long intestinal tube in patients with SBO.

**Table 1:** Outcomes of long-tube insertion by the transnasal ultrathin endoscopy method (Group A) and the conventional endoscopy method (Group B).

| | Group A (n = 29) | Group B (n = 32) | P value |
|---|---|---|---|
| Procedure time (Mean ± SD, min) | 15.3 ± 2.5 | 22.9 ± 2.4 | < 0.001 |
| Success rate (%) | | | |
| Total | 100 (29/29) | 93.8 (30/32) | 0.493 |
| No history of Billroth II anastomosis | 100 (25/25) | 100 (27/27) | |
| History of Billroth II anastomosis | 100 (4/4) | 60 (3/5) | 0.444 |
| Complications | | | |
| Bleeding of GI tract | 0 | 2 | 0.493 |
| Perforation | 0 | 0 | |
| Epistaxis | 8 | 7 | 0.767 |

**Aims & Methods:** To investigate and compare the effect on small bowel obstruction (SBO) of a long intestinal tube inserted by two different endoscopic placements which are transnasal ultrathin endoscopy and conventional endoscopy. Twenty-nine patients who had been diagnosed as suffering from SBO underwent long tube insertion placed by transnasal ultrathin endoscopy were included as subjects. Thirty-two patients who had undergone insertion of a long tube placed by conventional endoscopy were included as controls. The success rate of intubation of the small bowel, the time required for the procedure, and complications were compared between the subjects and controls.
**Results:** The outcomes of long-tube insertion by the transnasal ultrathin endoscopy method (Group A) and the conventional endoscopy method (Group B) are listed in table 1. The success rate of intubation was 100% (29/29) in subjects and 93.8% (30/32) in controls, without a significant difference (P = 0.493). There are 2 failed cases that the procedure was attempted near 60 min in 2 patients who had performed Billroth II anastomosis before, and the intestinal tube could not be inserted into efferent loops of jejunum in controls. The mean time required for the procedure was 15.3 min in subjects and 22.9 min in controls, respectively, and with a significant difference (P < 0.001). Epistaxis occurred in both groups, and 2 cases encountered bleeding of the gastrointestinal tract in controls.
**Conclusion:** Long tube insertion facilitated by transnasal ultrathin endoscopy takes shorter time and has a higher success rate compared with the procedure conducted with the help of conventional endoscopy. It is safe and useful to insert a long intestinal tube assisted by transnasal ultrathin endoscopy for the decompression of small bowel.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0127 RISK FACTORS FOR RECURRENCE OF UPPER GASTROINTESTINAL BLEEDING

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**Introduction:** Upper gastrointestinal bleeding (UGIB) is a frequent cause of hospitalization with significant morbidity.
**Aims & Methods:** The aim of this study was to evaluate the performance of Blatchford and Rockall score to predict in-hospital and post-discharge rebleeding and evaluate the clinical and laboratorial variables that are associated with a higher risk of rebleeding. We performed a retrospective observational study of patients undergoing upper gastrointestinal endoscopy for UGIB between January and December 2015.
**Results:** A total of 158 patients (92 men and 66 women) were included, with an average age of 71.8 ± 14.8 years. The most common aetiology of UGIB was peptic ulcer. Of the 158 patients, 8.3% had rebleeding during the hospitalization and 7% post-discharge. Overall, in-hospital and post-discharge mortality rate were, respectively, 10.1% and 1.3%. Hospitalized patients with shock criteria (P = 0.001), low average systolic blood pressure (103.8 vs. 120.1; P = 0.007) and

who needed more blood transfusions (4.6 vs. 1.4; $P < 0.001$) were more likely to have rebleeding. After discharge, patients with shock criteria ($P = 0.001$), diagnosis of cirrhosis ($P = 0.001$) and with comorbidities (81.8% vs. 50.3%; $P = 0.044$) were more likely to have rebleeding. In terms of in-hospital rebleeding, the area under the ROC curve was 0.680 (CI: 0.554–0.806) for Blatchford score, 0.686 (CI: 0.552 to 0.820) for admission Rockall score and 0.725 (CI: 0.612–0.839) for full Rockall score. In terms of post-discharge rebleeding, the area under the ROC curve was 0.640 (CI: 0.489–0.790) for Blatchford score, 0.629 (CI: 0.468–0.790) for admission Rockall score and 0.663 for full Rockall score (CI: 0.481–0.845).
**Conclusion:** The full Rockall score had a reasonable performance in predicting in-hospital rebleeding, compared with the remaining scores. After discharge, neither Rockall or Blatchford score were capable to predict rebleeding. The presence of shock, high number of blood transfusions and systolic blood pressure amount were clinical variables associated with higher potential of rebleeding.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0128 INGESTED FOREIGN BODIES AND FOOD IMPACTIONS: RETROSPECTIVE ANALYSIS OF 383 CASES

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**Introduction:** The resolution of food impactions (FI) and the removal of ingested foreign bodies (IFB) is a frequent indication for esophagogastroduodenoscopy in the Emergency Department [1]. Its rapid diagnosis and proper management are crucial to minimize morbidity.
**Aims & Methods:** The aim of this study was to characterize clinically and endoscopically the patients undergoing therapy for FI and/or IFB. This a retrospective study in a single center (2010–2015) including patients undergoing esophagogastroduodenoscopy due to FI/IFB. Data related to demographic parameters, treatment choices and complications of this group of patients were evaluated. Statistics analysis were performed using IBM SPSS Statistics 22 with $p < 0.05$ deemed to be statistically significant.
**Results:** We identified 384 patients, mostly male (53.4%) with mean age of $61.5 \pm 11.4$ years. FI was diagnosed in 66% of cases, and the IFB (34%) mostly identified were: fish (18%) or animal (16%) bones. The median period between the IFB/FI and the time the patient arrived to the Emergency Department was 6 hours (IQR: 2-12). There was no correlation between the location of the IFB sensation described by the patient and the endoscopic findings (Kappa value = 0.018). In 99.2% of the cases the successful endoscopic therapy was possible, with a perforation rate of 1.0% ($n = 4$). Forty-four percent of the patients had esophageal abnormalities, the most frequent were: Schatzki ring (22.2%) and benign esophageal strictures (18.1%). Fifteen percent of the patients had more than one episode of FI and/or IFB, and the presence of structural changes was associated with more than one event with an OR = 7.790 (95% IC: 3.449-17.598). The presence of minor complications (superficial laceration, self-limiting bleeding) after FI/IFB resolution occurred in 30.3% of the patients. The presence of minor complications was higher among patients who had FI vs. IFB (52.3% vs 17.7%, $p < 0.001$). The use of foreign body grasper in comparison to roth net foreign body retrieval was associated with higher frequency of minor complications (59.1% vs. 22.5%, $p < 0.001$). However, a linear regression model concluded that the type of IFB was independent of the tool used (roth net or grasper) for the presence of minor complications.
**Conclusion:** Endoscopic resolution of FI/IFB was associated with a low rate of major complications. Regardless of the tool used for endoscopic therapy, complications were more frequent in FI than in the IFB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0129 ENDOSCOPIC FULL-THICKNESS RESECTION OF UPPER AND LOWER GASTRO-INTESTINAL LESIONS USING A NEW, FLAT BASED OVER-THE-SCOPE-CLIP; A FEASIBILITY STUDY

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**Introduction:** Surgical resection of subepithelial tumors (SET) in the stomach and duodenum and incompletely resected colonic adenomas is associated with significant morbidity and mortality. A new over-the-scope-clip (Padlock) mounted on a transparent cap can be used for endoscopic full-thickness resection (eFTR). The flat base of the clip is thought to facilitate full-thickness resection, obviating the need for surgery.
**Aims & Methods:** We evaluated the feasibility and safety of eFTR using the Padlock clip for gastric, duodenal and colonic lesions. After successful clip placement, lesions were removed with a snare in auto-cut mode. Patients were observed for one night after the procedure. Patients were followed for one month to assess severe adverse events (SAEs); 3–6 months after eFTR, endoscopy was performed. eFTR was performed on 22 lesions in 21 patients: 6 gastric SETs (10–18 mm) with proven histology of a gastro-intestinal stromal tumor (GIST) or inconclusive histology; 6 duodenal (suspected) subepithelial neuroendocrine tumors (4–13 mm); 10 colonic adenomas (5 incompletely resected adenomas, 4 recurrent non-lifting adenomas, and 1 adenoma in a diverticulum).
**Results:** Technical success was achieved in 19 cases (86%); 2 gastric lesions could not be positioned within the cap and in one patient, the endoscope could not pass the pharynx. In all 19 cases, histology confirmed that full-thickness resection was achieved. Histology of the gastric lesions revealed GIST ($N = 1$) and ectopic pancreas ($N = 2$). In the duodenum, gastrinoma ($N = 3$), brunneroma ($N = 1$) and ectopic pancreas ($N = 1$) were seen. Colonic specimens showed scar tissue ($N = 7$), low grade dysplasia ($N = 2$) and adenocarcinoma ($N = 1$). No SAEs were observed after resection of gastric lesions. Two resections in the cecum were complicated by (micro) perforation; one was treated conservatively with antibiotics, the other was treated with laparoscopic suturing. After duodenal resection, several SAEs were observed: perforation ($N = 2$), severe pain ($N = 2$), and hemorrhage ($N = 1$). During follow up endoscopy, the clip was no longer in situ in the majority of available patients (6/8; 75%). The mucosa was healed in all patients and no recurrence was observed in biopsies of the scars.
**Conclusion:** eFTR with this new flat-based, over-the-scope-clip is feasible and effective. Full-thickness resection was achieved in all patients, but was accompanied by a significant risk of perforation. Therefore, the design of the clip and the technique of the resection need further refinement to improve safety of resection of SET and recurrent adenoma, in particular in thin walled areas such as the duodenum and cecum.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0130 ENDOSCOPISTS' BIOPSY RATE (EBR) AS A QUALITY INDICATOR FOR DIAGNOSTIC OUTPATIENT GASTROSCOPY

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**Introduction:** Many of gastric cancers arise from precancerous lesions which are commonly missed at endoscopy. A quality indicator for detection of premalignant lesions and early cancers at gastroscopy is urgently needed. Detection of these lesions in conventional endoscopy relies on biopsy sampling of suspicious areas in the stomach. We hypothesized that the rate of biopsies at gastroscopy varies among endoscopists and this rate is associated with a likelihood of detecting premalignant lesions.
**Aims & Methods:** The aim was to investigate a variability in taking biopsies by endoscopists and to analyze association between endoscopists' biopsy rate (EBR) and detection of dysplastic lesions and all premalignant conditions (atrophic gastritis, intestinal metaplasia and dysplasia) at diagnostic outpatient gastroscopy. This was a cross-sectional study analyzing outpatient gastroscopy data and histopathology reports from a single academic endoscopy unit in Poland between years 2002 and 2010. Procedures with indications of surveillance for already known premalignant conditions (Barrett's esophagus, atrophic gastritis, gastric intestinal metaplasia and dysplasia), genetic cancer syndromes (familial adenomatous polyposis and Lynch syndromes) and history or suspicion of upper gastrointestinal (UGI) cancers at other imaging tests were excluded from analysis. We have also excluded gastroscopies performed by endoscopists who did less than 100 procedures during the study period. For each endoscopist we counted biopsy rate as a percentage of endoscopies with at least one biopsy for histopathological examination obtained (ICD-9 codes 45.14, 45.16, 42.24) to all performed gastroscopies (EBR). Biopsies for rapid urease test were not included. After setting a median value of EBR as the cut-off point we divided endoscopists

into low and high EBR groups. We analyzed association between EBR group and detection of dysplasia and premalignant conditions at gastroscopy using multivariate clustered logistic regression model adjusted for patients' age and sex.
**Results:** Of the total 17, 490 gastroscopies 4, 690 (26.8%) met exclusion criteria and the remaining 12, 800 procedures performed by 16 staff endoscopists were analyzed. The EBR varied from 19% to 62% between endoscopists with median value of 39% by which we assigned 8 endoscopists to low and 8 to high EBR groups. In total, 86 (0.7%) gastric dysplasia and 1013 (7.9%) all gastric precancerous lesions were detected. The adjusted odds ratio for detecting gastric dysplasia or any precancerous lesion in the high EBR group were 1.79 (95%CI, 1.13–2.83; $P = 0.012$) and 2.20 (95%CI, 1.91–2.53; $P < 0.001$) respectively, as compared to the low EBR group.
**Conclusion:** Biopsy rate is highly variable among endoscopists. Endoscopists with high EBR detected significantly more dysplastic lesions and over twofold more precancerous lesions in the stomach than those with low EBR. EBR is a candidate EGD quality indicator.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0131 ENDOSCOPIC ZENKER DIVERTICULOTOMY USING THE WINDOW TECHNIQUE: A TECHNICAL TRICK TO IMPROVE THE FIELD OF VIEW

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**Introduction:** Zenker's diverticulum is a protrusion of the hypo-pharyngeal mucosa through a weak area between the inferior pharyngeal constrictor muscle and the cricopharyngeal muscle, responsible of symptoms such as dysphagia, regurgitations, night cough and in the worst cases loss of weight and pulmonary infection. It can be treated by surgery with external myotomy of the cricopharyngeal muscle and removal of the diverticulum or by endoscopic procedure with division of the muco-muscular septum between the diverticulum and the esophagus. Endoscopic diverticulotomy is a safe, effective, and simple technique [1] and was demonstrated to be as effective as surgical external diverticulotomy in most cases and can be recommended as the first choice [2]. Diverticuloscope-assisted diverticulotomy has been demonstrated to be safer and more effective than the cap-assisted procedure [3]. The main benefit of the diverticuloscope is to improve exposure of the muscular fibers by stretching them [4]. In our practice, we additionally use a technical trick called the ''window technique'' by doing a mucosa window at the top of the septum to improve the field of view before the myotomy. We are currently studying the feasibility of this trick, the technical and clinical results, in our department.
**Aims & Methods:** Are included, retrospectively, all patients treated for symptomatic Zenker's diverticulum in our department, by endoscopic diverticulotomy using this technical trick, since december 2008. After insertion of the diverticuloscope, we initially cut a small square of mucosa to enlarge the space and expose the muscular fibers. This step usually takes 1 minute. A square, measuring approximately 5 mm, is cut on the four sides and then removed. We usually use a Hook-knife to create this window with Endocut electric current. Thanks to this mucosal window, the cricopharyngeal fibers are stretched and visible. Without the mucosal window, the two sides of the sectioned mucosa can obscure the myotomy site and prevent perfect control of the depth of cutting. In contrast, the mucosal window helps to enlarge the field of view and allows us to precisely catch the muscular layer by hooking. To evaluate long-term results, phone interview were made.
**Results:** Currently, 46 patients are included, 27 males (59%) and 19 females (41%), median age is 68 years (34-98y), and 50 endoscopic diverticulotomy were performed, by 4 different endoscopists (4 patients had 2 procedures because of recurrent or persistent symptoms). Main symptoms were dysphagia (93.5%), regurgitations (69.6%), loss of weight (34.8%), gastric reflux (34.8%), night cough (17.4%) and pulmonary infection (13%). Mean depth of diverticulum was 4.5 cm (0.5–9 cm), 37 procedures (74%) were diverticuloscope-assisted and 7 were cap-assisted (14%) (Missing data $n = 4$). Mean time of the complete procedure was 43 minutes (14–76). At the end of procedure, 1 to 3 clips were placed to prevent secondary perforation or bleeding. 35 patients (76%) could resume drinking within 24 hours and 39 (85%) mixed diet within 48 hours after procedure. Mean hospitalization time was 3, 7 days (2–13 days). One patient with anticoagulation therapy had delayed haemorrhage 2 days after procedure, treated with efficacy by endoscopic haemostasis. Two patients presented mild mediastinitis, treated by antibiotics with favourable evolution and were discharged after respectively 7 and 10 days. So far 27 patients were contacted to evaluate long term results (59%), (1–72 months), the clinical efficacy is 88.9% the first month, 85.1% the second month and 78% at the end of the actual follow up. 4 patients (8.7%) had a second procedure, for a recurrent diverticulum or persistent symptoms due to an insufficient section of the septum.
**Conclusion:** Patients are still being included and many remain to be contacted to evaluate clinical efficacy, but so far, this work indicates that endoscopic diverticulotomy is effective, safe and the window technique is a simple and feasible trick to facilitate the myotomy by enlarging the field of view and allowing us to precisely catch the muscular layer, leading to a complete section.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0132 ENDOSCOPIC DOUBLE-LAYER SUTURE FOR THE GASTROINTESTINAL WALL DEFECT AFTER FULL-THICKNESS RESECTION

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**Introduction:** Successful closure of gastrointestinal (GI) wall defects is the key procedure following endoscopic full-thickness resection (EFR).
**Aims & Methods:** To describe a new endoscopic closure method for gastrointestinal wall defects after EFR procedure similar to hand-sewn double-layer suture technique–endoscopic double-layer suture (EDS) and evaluated the safety and efficacy of this method. We retrospectively analyzed 15 patients who presented at our institute between April 2011 and September 2015 with GI tumors (13 of gastric subepithelial tumors, 2 of colonic lateral spreading tumors) and who underwent EFR, with the resulting full-thickness wall defects being closed using EDS technique. The seromuscular and mucosal layers of wall defects were sutured separately by using endoclips with or without endoloops assistance during EDS procedure. Tumors characteristics, en bloc resection rates, suturing procedures and complications were evaluated in all patients.
**Results:** Successful en bloc resection and closure of wall defects were achieved in 15 cases (100%). The mean maximum size of lesions was 2.4 cm (range 1.0–3.3 cm). The mean size of wall defects after EFR was 2.1 cm (range 0.8–3.5 cm, $\geq 2.5$ cm in 6 cases and $< 2.5$ cm in 9). The total mean closure time was 54.9 min (range 18–106 min), the mean closure time was 82.7 min (range 62–110 min) in $\geq 2.5$ cm group and 36.4 min (range 18–60 min) in $< 2.5$ cm group ($P = 0.01$). The mean number of endoclips during EDS was 26.7 (range 17–58) including 10.6 (range 5–26) in seromuscular closure and 16.1 (range 10–32) in mucosal closure. The suture procedure with endoloops assistance was completed in 7 patients (46.7%). Histological diagnosis was gastrointestinal stromal tumor (GIST) in 8 lesions (4 fundus, 2 bodies, 2 antrum;), schwannoma in 3 lesions (2 fundus and 1 antrum), heterotopic pancreas in 1 lesion (antrum), cystic fibroma in 1 lesion (fundus) and early colonic adenocarcinoma in 2 lesions. Five patients developed localized peritonitis after treatment, 3 cases of postoperative peritonitis resolved after antibiotic treatment and two cases required placement of an abdominal tube for continuous peritoneal lavaged 3 days without surgical intervention. No patient developed delayed hemorrhage, abdominal abscess and chronic fistula after the procedure. During the mean follow-up time of 19.1 (range 3–52) months, wounds healed in all cases and no tumor recurrence was found in any patients.
**Conclusion:** EDS is relatively safe and effective method for repairing GI wall defects resulting from EFR. The new closure method mimics hand-sewn double-layer suture technique during surgical procedure. However, EDS for closure of $\geq 2.5$ cm GI wall defect is more time consuming, further control study is required to evaluate the efficacy of this method compared with other endoscopic GI defect suture methods.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0133 ENDOSCOPIC SEPTOTOMY IS A NOVEL TREATMENT FOR CHRONIC LEAKS COMPLICATING LAPAROSCOPIC SLEEVE GASTRECTOMY

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**Introduction:** Staple-line leak following laparoscopic sleeve gastrectomy (LSG) is a dire adverse event. The leading etiology is sleeve stenosis leading to increased pressure in the proximal stomach that exceeds the burst-pressure of the staple line. While the treatment of acute and early leaks is well established, there is still dispute regarding late and chronic leaks, (6–12 and $> 12$ weeks after surgery, respectively) with paucity of data regarding endoscopic treatment. Late and chronic leaks are characterized by a well-defined, walled-off perigastric space with a feeding fistula. As a result the clinical course is usually insidious with no overt sepsis. Endoscopic treatment should address these chronic changes and the precipitating factors. We describe a novel approach combining septotomy and sleeve stricture dilatation for treating late/chronic leaks.
**Aims & Methods:** All patients with late/chronic leaks referred to our clinic during 2014–2015 were treated endoscopically. The septum separating the sleeve lumen from the perigastric cavity was progressively dissected using argon plasma coagulation. Downstream strictures underwent pneumatic dilatation. (Rigiflex 30 mm 20PSI, Boston Scientific). Success was defined as avoiding further surgical intervention, removal of external drain tubes and weaning from parenteral nutrition.
**Results:** Ten consecutive patients were treated. Average time between surgery and first endoscopic treatment was 202 days. All leaks were located at the Angle of His. Sleeve stricture was diagnosed in 8 patients, in whom a septotomy accompanied by stricture dilatation was performed. A mean of 5 sessions over the course of 43 days was needed to complete endoscopic treatment. In the remaining 2 patients a small perigastric cavity was diagnosed without downstream stricture, and the septotomy was achieved with through-the-scope balloon dilatation of the fistula. No adverse events were encountered. Nine patients (90%) were treated successfully. One patient developed recurrent leak 3 months after end of treatment and was referred to surgery.

**Conclusion:** Septotomy accompanied by pneumatic stricture dilatation seems highly effective and safe in late/chronic leaks following LSG and may prevent further major surgery with high co-morbidities rate.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0134 UPPER GASTROINTESTINAL ENDOSCOPY IN GRAFT-VERSUS-HOST DISEASE

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**Introduction:** Receptors of allogeneic hematopoietic cell transplantation (alloHCT) often develop graft-versus-host disease (GVHD) with cutaneous, digestive and other manifestations.
**Aims & Methods:** The aim of this study was to analyze the role of upper endoscopy (EGD) in alloHCT patients who presented with upper gastrointestinal symptoms. Methods: retrospective study of patients undergoing alloHCT from January 2012 to December 2015 that were submitted to EGD.
**Results:** 63 patients were included among those submitted to alloHCT in our institution (n = 275), 51% male and mean age of 37 ± 18 years. All patients were on GVHD prophylaxis and 21% were already under treatment, although the majority (74%) had not previously diagnosed GVHD. The main complaints were nausea (67%) followed by vomiting (57%), anorexia (46%), dysphagia (11%) and dyspepsia (9%); diarrhoea was also present in 56% of cases. All patients underwent biopsies of at least one segment, even in the absence of endoscopic alterations (28%). The second duodenal portion was submitted to biopsies in 96% and the stomach in 85%. Although no endoscopic findings predicted the diagnosis of GVHD, an endoscopic Correa score $\geq 2$ was associated with histological confirmation of GVHD ($p < 0.001$), with 81% sensitivity and 78% specificity for diagnosis. However, in 5 cases without positive endoscopic findings, biopsies confirmed GVHD and EGD with biopsies additionally allowed the identification of 20 cases previously undiagnosed. After the EGD, 49% of patients had upgrade of therapy, with clinical improvement resulting in a similar proportion.
**Conclusion:** EGD favorably modifies the management of about half of alloHCT patients with digestive complaints, being useful not only in confirmation of the clinical diagnosis or suspicion but also for the identification of new cases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0135 DIAGNOSIS OF TUMORS IN THE CERVICAL AND UPPER THORACIC ESOPHAGUS: EFFICACY OF ENDOSCOPIC ULTRASONOGRAPHY USING A JELLY-FILLING METHOD WITH WATER-SOLUBLE LUBRICATING JELLY; A RETROSPECTIVE SINGLE-CENTER TRIAL

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**Introduction:** Endoscopic ultrasonography (EUS) is the standard modality for qualitative diagnosis of submucosal tumors (SMTs) and determining the depth of invasion of esophageal cancer. Standard EUS, however, comprises a continuous water-filling or water-filled balloon method, which creates some problems (e.g., difficulty filling the water, poor image quality because of balloon compression, water aspiration). Water aspiration is especially problematic during the diagnosis of lesions in the esophagus adjacent to the hypopharynx. Therefore some endoscopists are skeptical about performing EUS for lesions in the cervical and upper thoracic esophagus.
To resolve such disadvantages, we reported a method using probe EUS with a jelly-filling technique (EUS-J) to evaluate superficial esophageal squamous cell carcinomas (SCCs). The procedure is characterized by filling the esophageal lumen with a water-soluble lubricating jelly (K-Y lubricating jelly; Johnson & Johnson, Tokyo, Japan) that is used for routine endoscopy and is harmless to humans; this enables convenient observation without the use of a balloon. More recently, we retrospectively evaluated the usefulness of EUS-J with water-soluble lubricating jelly for lesions in the cervical and oral side of upper thoracic oesophagus.
**Aims & Methods:** Patients with an esophageal SCC or SMT in the cervical (18 cm from incisors) or oral side of upper thoracic oesophagus (18 ~ 21 cm from incisors) were included. EUS-J with water-soluble lubricating jelly was performed using a high-resolution probe. Before examination, several 5-mL syringes containing the water-soluble lubricating jelly were prepared. With the patient under conscious sedation with midazolam, an endoscope (GIF-2TQ260M; Olympus, Tokyo, Japan) was inserted into the targeted area in the esophagus. A 30- or 20-MHz miniature probe was then inserted through the left channel of the endoscope, and 40 mL of jelly was instilled through the right channel until the esophageal lumen was filled. For esophageal SCCs, the diagnostic accuracy of EUS was analyzed while the histologic diagnosis of resected specimen served as reference standard.
**Results:** From December 2010 to April 2016, we used EUS-J to evaluate 28 patients with esophageal SCCs and 10 with SMTs in the cervical or oral side of upper thoracic esophagus. There were 10 lesions in the cervical esophagus and 28 in the oral side of upper thoracic esophagus.
Among the 28 SCCs, 7 were recurrences following chemoradiotherapy. The other 19 SCCs did not undergo chemoradiotherapy. All 28 esophageal SCCs lesions were detected with EUS-J. 21 lesions treated either by esophagectomy (n = 3) or endoscopic resection (n = 18). Histologic diagnosis was T1a in 12 lesions, T1b in 9 lesions. The overall accuracy of diagnosing invasion depth was 76.2% (16/21 lesions) by EUS.
Among the 10 SMTs were seven leiomyomas derived from muscularis mucosa and one lesion due to vertebral body compression. The other two lesions were a tiny SMT (< 3 mm) and a small lesion in the cervical oesophagus adjacent to the hypopharynx. Neither was detected by EUS-J because of their small size and difficult instrumental manoeuvering. There were no adverse events with EUS-J.
**Conclusion:** EUS-J with water-soluble lubricating jelly is useful and safe for diagnosing lesions in the cervical or oral side of upper thoracic esophagus.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0136 THE STUDY OF THE RESULTS OF DUODENOSCOPE CHANNELS BY DIFFERENT DISINFECTION METHODS

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**Introduction:** In China, the number of procedures involving duodenoscope use is increasing each year since ERCP is one of the best ways of resolving various problems caused by cancer, gallstones, or other conditions in the pancreatic and biliary ducts. However, physicians have not paid much attention to duodenoscope-related (especially the elevator channel and biopsy channel) infection so far. For the clinical various strains of drug-resistant strains increase, variation, cleaning and disinfection of endoscope has become a high-profile topic. Recent reports regarding duodenoscope-related infections raised many concerns to healthcare community worldwide. The purpose of this article is to compare the clump count of elevator channel and biopsy channel, to explore the situation of bacterial contamination of duodenoscope channels.
**Aims**: To study the effect of the different kinds of methods disinfecting duodenoscope channels (the biopsy channel and the elevator channel).
**Methods**: 30 samples were measured randomly from 20th Oct, 2015 to 17th Nov, 2015 in a grade A tertiary Hospital, Shanghai. Group A (N = 10), using the automatic cleaning sterilizer with OPA. Group B (N = 10), using manual cleaning and disinfection with OPA. Group C (N = 10), using the automatic cleaning sterilizer with peracetic acid. Collected and compared the data of bacterial colonies number of different groups, analyzed by SPSS19.0.
**Results:** The disinfection eligible rate of duodenoscope is 16.67%. There is no difference between the clump count of biopsy channel and elevator channel among three groups ($P > 0.05$). The elevator channels' bacterial colonies number of group A are higher than that of group C ($P < 0.05$). The elevator channels' bacterial colonies number of group A are higher than that of group B ($P < 0.05$).
**Conclusion:** The disinfection eligible rate of duodenoscope is low. There is no distinction between the clump count of biopsy channel and elevator channel with different cleaning and disinfection methods. For the elevator channel, using peracetic acid is better than OPA (in the same "automatic cleaning sterilizer" condition), and manual cleaning and disinfection is better than automatic cleaning sterilizer under the same "using OPA" condition.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0137 ERGONOMICS OF ENDOSCOPY: PRE AND POST VIDEO TRAINING EVALUATION OF GI FELLOWS' AWARENESS OF OCCUPATIONAL INJURY DUE TO ENDOSCOPY AND BEST PRACTICES FOR PREVENTION

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**Introduction:** Gastroenterologists often experience musculoskeletal injury as a result of repetitive strain during endoscopic procedures. Survey data has reported the prevalence of musculoskeletal pain/injury among endoscopists at 29%-89%. Little information is available regarding such injuries to trainee GI fellows and their training to prevent injury due to endoscopy.
**Aims & Methods:** To ascertain GI fellow awareness of occupation injuries and the value of video training instruction of best practices to minimize injury from performing endoscopy. A written and online survey was distributed to GI fellows at 12 US training programs and an international group of fellows using an email distribution group in Spain and the UEG Young GI Fellows Facebook group. After a 30 question pre-test, a 6 minute teaching video regarding endoscopy ergonomics and practice patterns to minimize injury. This was followed by an 8-question post-test. The questionnaire evaluated knowledge of occupational injury, previous training and basic demographic information.
**Results:** 99 fellows completed the training, 63% were male. 51% (50/99) participated via lecture attendance. Fellows trained in the United States (92), Spain (7) and Romania (1). Fellows were evenly divided by level of training across first three years: first (35%), second (25%) and third (29%). European training with final year, fourth year fellows (4%) and advanced US fourth year fellowship training (4%) were a minority. A majority had performed more than 150 EGD's (68%) and 150 colonoscopies (61%). 77% (76/99) were concerned about developing musculoskeletal injury related to endoscopy but only 8% reported training as part of their curriculum, which was sporadic and more commonly in the form of individualized attending teaching during endoscopy (56%) and one-third reported no training. GI fellows reported musculoskeletal pain attributed to endoscopy at an alarmingly high rate (71%) with the most common sites being the hand (38%), wrist (37%), thumb (32%) and neck (32%). No treatment was required for 70% of the time. Only 2 fellows had to miss work due to injury, but 18% have had to reduce physical activity outside of the hospital due to an endoscopy-related injury. Post-test data after viewing a short training video demonstrated an overall 12% increase in correct responses. Over 90% of respondents felt their curriculum should incorporate endoscopic ergonomic and injury prevention training.
**Conclusion:** The majority of GI fellows reported endoscopy-related musculoskeletal injury, with nearly one-fifth requiring a reduction in physical activity. Less than 10% of the fellowship program curricula included ergonomic training; however, over 90% of fellows were in favor of inclusion. Video-based training may provide an effective resource. Further study of injury patterns in trainees and the long-term impact of endoscopic ergonomic training on occupation-related injuries is warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0138 OBSERVER AGREEMENT AMONG NOVICES IN IMAGE ASSESSMENT OF BARRETT'S ESOPHAGUS USING A SIMPLIFIED NARROW-BAND IMAGING CLASSIFICATION: A RETROSPECTIVE MULTI-CENTER STUDY

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**Introduction:** We demonstrated the usefulness of a simplified narrow-band imaging (NBI) classification of surface patterns in Barrett's esophagus (BE) using high-definition magnification endoscopy with NBI (HDME-NBI) (Kato M, et al. UEGW 2014). It is, however, unclear whether this classification is useful for novices. We conducted this study to validate the interpretation of the NBI classification among novices.
**Aims & Methods:** A total of 248 HDME-NBI images from non-dysplastic and flat-type dysplastic areas in 89 patients with BE were retrieved and randomized for review by eight novices (endoscopists who experienced more than 200 procedures of white-light endoscopy and none of experience of magnification endoscopy). All novices took the 1st exam before receiving the lecture about the classification, the 2nd immediately after the lecture, and the 3rd six weeks after the lecture. The primary endpoint was observer agreement of NBI surface patterns and predicted histology (dysplasia vs. non-dysplasia), and the secondary endpoint was the classification-based diagnostic accuracy values.
**Results:** The overall inter-observer agreements were all substantial for mucosal pattern ($\kappa = 0.78$), vascular pattern (0.70) and predicted histology (0.79) in the 2nd exam. The overall intra-observer agreements were almost perfect for mucosal pattern (0.81) and predicted histology (0.81) and substantial for vascular pattern (0.78) between the 2nd and 3rd exams. Although the mean values of sensitivity, specificity and overall accuracy for all novices in the 1st exam were 86.6%, 80.0% and 82.0%, respectively. The mean values of sensitivity, specificity and overall accuracy in the 2nd exam were 87.2%, 96.9% and 94.1%, respectively.
**Conclusion:** The simplified NBI classification seems to be easily understandable and reliable and to have high diagnostic accuracy for novices.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0139 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL PROXIMAL ESOPHAGEAL NEOPLASIA IS HIGHLY SUCCESSFUL

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**Introduction:** Squamous-cell carcinoma accounts for about 90% of all esophageal cancer cases in China and worldwide. It is most commonly found in the upper and middle esophagus. Esophagectomy is a procedure with a high morbidity and mortality. Surgery for a tumor located in the proximal esophagus is a technically challenging procedure and carries a higher then average morbidity and mortality compared to other esophageal procedures. Following a successful esophagectomy, most patients experience disabling symptoms, such as regurgitation and dysphagia. Therefore, it is common for radiation therapy alone to be recommended for patients with the proximal carcinoma of esophagus. Endoscopic submucosal dissection (ESD) was developed in Japan by Gotoda et al to permit the en bloc resection of large flat rectal lesions. Subsequently, ESD was used for therapy of early gastric cancer and esophageal lesions. Compared to surgery, ESD is an incisionless, minimally invasive, endoscopic treatment aiming to cure early neoplasia of the gastrointestinal tract. It is performed worldwide because of its perioperative safety and excellent short and long-term outcomes. However, the narrow lumen and thin wall of the esophagus, movement caused by respiration and heartbeats make it difficult to perform ESD for the proximal esophagus. There is no publication about ESD for the treatment of superficial proximal esophageal neoplasia. The aim of our study was to assess the feasibility, safety and long-term outcome of the ESD procedure for treatment of superficial proximal esophageal neoplasia.
**Aims & Methods:** Squamous cell cancer of the esophagus accounts for 90% of malignant esophageal neoplasia cases worldwide. Superficial esophageal neoplasia located in the cervical and upper thoracic region is uncommon. The surgery for a tumor located in this region, due to a complicated anatomy, is very difficult and leads to a high morbidity and mortality. Endoscopic submucosal dissection (ESD) is a minimally invasive endoscopic treatment of superficial neoplasia of the gastrointestinal tract allowing en bloc resection with low recurrence rates. The aim of this study was to evaluate the outcomes of ESD for superficial proximal esophageal neoplasia. We retrospectively analyzed 102 consecutive patients that fit the inclusion criteria with 106 lesions who underwent ESD from February 2009 to July 2015 at the Zhongshan Hospital, Fudan University in Shanghai, China. During the study the en bloc and pathologically complete resection rates, complication rate, incidence of esophageal stricture after ESD, disease-specific and overall survival rates were evaluated.
**Results:** The mean age was 62 (45–84) years with100% en bloc resection rate. The mean operation time was 48 (10–144) minutes. The mean diameter of the resected tumors was 2.9 (1.2–6.5) cm. The pathological diagnoses were high grade intraepithelial dysplasia in 45 (42.5%) lesions, rest were squamous cell carcinoma with staging of intraepithelial in 18 (17.0%), lamina propria in 13 (12.3%), muscularis mucosa in 16 (15.1%), SM1 in 10 (9.4%) and SM2 or deeper in 4 (3.8%) of the lesions. The R0 resection rates were 94.3% (100/106). There was no delayed bleeding. Two small perforations observed were closed successfully with clips. Symptomatic esophageal strictures in 17 patients were treated by endoscopic

balloon dilation with a mean of 4 (1–14) times and 88.2% (15/17) success. Additional treatments of esophagectomy or chemoradiotherapy were recommended to patients with sm1 or deeper neoplasia or incomplete resection. Local recurrence was observed in three (2.9%) cases. 15 patients were lost to follow-up. 5-year overall survival rate was 98% and disease-specific survival rate was 100%. The mean follow-up time was 33.6 months.
**Conclusion:** ESD for the superficial proximal esophageal neoplasia is a safe and a very effective treatment method with a 100% 5 year disease specific survival rate.
**Disclosure of Interest:** All authors have declared no conflict of interest.

## P0140 DETECTION OF NEOPLASIA IN BARRETT'S DISEASE WITH IMAGE ENHANCEMENT USING OE– AN EARLY EXPERIENCE

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**Introduction:** Barrett's esophagus (BE) is the metaplastic transformation of the esophageal squamous mucosa to intestinal columnar mucosa with the potential for malignant transformation. Current surveillance protocols recommend standard white light endoscopy and 4 quadrant biopsies every 1–2 cm. However, areas of dysplasia may not be visible on standard white-light examination. Multiple biopsies still carry a risk of sampling error and are time-consuming and costly. Recent advances in image enhancement technology have been proposed as potential alternatives to allow accurate detection and targeted biopsies. The ASGE PIVI statement states that any imaging technology for BE surveillance should achieve per- patient sensitivity >90% and a negative predictive value of 98% or greater. Most technologies that are available and have been tested in this area have struggled to achieve this high threshold. Disadvantages of existing technology include poor spatial resolution in surveying long segments of BE and the ability to combine morphological data with details of vascular architecture. OE is a new technology that combines the ability to analyse microvascular pattern using band limited light with digital chromo endoscopy. In OE1 mode spectral transmission utilises the peak wavelength of the haemoglobin absorption spectrum thereby enhancing surface vessel pattern. OE2 mode adds in the longer wavelength of red light allowing more natural and brighter illumination. It is expected that the ability to combine detailed assessment of vascular and mucosal pit patterns at the same time will enhance increased detection and characterisation of neoplasia and assessment of margins of lesions discovered. The use of this technology in BE surveillance is as yet unstudied.
**Aims & Methods:** The aim of our study was to assess the sensitivity and Negative Predictive Value of OE in detecting neoplasia within segments of Barrett's disease. 10 patients with Barrett's oesophagus were assessed as part of the study. 6 of these individuals had established long segment BE with biannual surveillance. The rest were diagnosed with short segment disease and had less frequent surveillance. No patient had previously been diagnosed with definite dysplasia or undergone endoscopic therapy. One patient had cellular atypia associated with active inflammation reported during prior endoscopy. Barrett's mucosa was examined with high definition white light followed by OE1 and OE2 mode. Biopsies from any area of neoplasia identified by OE were reviewed by 2 pathologists.
**Results:** We did not discover visible abnormalities or changes suggestive of neoplasia in 8 of the 10 cases. Histopathology from the BE segment confirmed absence of dysplasia in all these patients. In one individual with long segment BE an area of focal high grade dysplasia was predicted on the basis of vascular anomalies on magnification endoscopy with OE. Biopsies from this area were confirmed by 2 pathologists as focal high-grade dysplasia. Another individual had ulceration noted within the segment of BE with vascular and epithelial alterations suggestive of reactive changes on OE and confirmed as such on histopathology. Diagnostic sensitivity was calculated for our 10 cases as 100% and similarly Negative Predictive Value for detection of neoplasia was estimated and is 100%.
**Conclusion:** Our early experience using OE in Barrett's disease suggests that this new image enhancement technology is promising in its ability to accurately detect neoplasia. In our limited case series it has been able to achieve the thresholds set by the PIVI statement. Further prospective studies are required with larger number of patients to assess the technology further and its utilisation in day to day clinical practice.
**Disclosure of Interest:** S. John: Author received travel grant from Pentax Medical 2 years ago.
H. Neumann: Author has received financial support from Pentax medical for travel and speaking.
All other authors have declared no conflicts of interest.

## P0141 DEVELOPMENT AND INITIAL VALIDATION OF A NEW ENDOSCOPIC TRAINING MODEL FOR ADVANCED ENDOSCOPIC PROCEDURES – THE HEAT INTERNATIONAL ENDOSCOPY STUDY

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**Introduction:** Hands-on training of advanced endoscopic procedures is of paramount importance. To date, training is mostly performed with animal models. However, due to the thickened mucosa and the diverging anatomical situation of the animal model, advanced endoscopic procedures are somehow difficult to teach and learn.
**Aims & Methods:** Primary objective was to develop and validate a new endoscopic training model designed for hands-on training of advanced and complex endoscopic procedures. In the first phase, human cadaver models were specially prepared for upper and lower gastrointestinal endoscopy. In the second phase, twelve endoscopists with different experience from seven different countries were trained in advanced endoscopic procedures, including ESD, POEM, sealing of perforations by using different types of hemoclips and the over-the-scope-clip (OTSC) and in endoscopic full thickness resection. Outcomes of endoscopic procedures performed during the study period were analyzed.
**Results:** A new interventional endoscopy training model for advanced endoscopic procedures with specially prepared human cadaver models was developed and validated in an international study. A significant improvement of the endoscopic skills was noted for all procedures performed, especially for ESD and POEM. Of note, perforations occurring during the study showed a real-life appearance and could be managed endoscopically therefore allowing completion of procedures in all cases. In addition, endoscopic full thickness resection was successfully performed by the participants. All participants rated training with the new model as significantly more effective compared to traditional training based on animal models.
**Conclusion:** The HEAT international endoscopy study was initiated to develop and validate a new endoscopic training model for advanced endoscopic procedures. Technical skills of the attending endoscopists improved rapidly and training was rated as more effective as traditional hands-on training with animal models. Based on the study results we now recommend to include the HEAT model in endoscopy training programs before advanced endoscopic procedures should be performed in living patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0142 A STUDY ON THE IMPACT FROM THE USE OF NAFAMOSTAT MESILATE, A SYNTHETIC PROTEASE INHIBITOR, AS AN ANTICOAGULANT FOR HEMODIALYSIS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION ON POST-ESD BLEEDING IN THE PATIENTS WITH END-STAGE RENAL DISEASE

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**Introduction:** Bleeding after gastric endoscopic submucosal dissection (ESD) is one of major complications. It is reported that end-stage renal disease on hemodialysis is important as one of the risk factors of bleeding after gastric ESD, but little reported about the methods to prevent bleeding after gastric ESD among hemodialysis patients.
**Aims & Methods:** Nafamostat mesilate (FUT) is a synthetic protease inhibitor with a short half-life and used as an anticoagulant for hemodialysis in the patients at high risk for bleeding instead of heparin because it does not prolong the systemic coagulation time. We evaluated the impact from the use of FUT for hemodialysis after gastric ESD on post-ESD bleeding. The 540 patients with 584 lesions who underwent gastric ESD between April 2004 and March 2016 in our institution were retrospectively analyzed. In hemodialysis patients, we temporally used FUT or low-molecular-weight heparin (LMWH) for hemodialysis after gastric ESD instead of heparin.
**Results:** Of all the patients who underwent gastric ESD, 54 (10.0%) had chronic kidney disease and 18 (3.3%) were undergoing hemodialysis. The mean period on hemodialysis was 5.8 ± 6.0 years, and the most causative disease getting on hemodialysis was diabetic nephropathy (50.0%). In hemodialysis patients, 10 (55.6%) took anti-platelet agents and 3 (16.7%) underwent double anti-platelet therapy. Bleeding after gastric ESD occurred in 46 (8.5%) of all the patients and 8 (44.4%) of hemodialysis patients. By multivariate analysis, end-stage renal disease on hemodialysis was strong risk factor of bleeding after gastric ESD (OR 4.75 [95%CI 1.24–19.9], p = 0.02), as with procedure in the lower thirds of the stomach (OR 2.40 [95%CI 1.24–4.85], p = 0.009). FUT was used for 15 (83.3%) and LMWH for 3 (16.7%) of hemodialysis patients after gastric ESD (because of 1 procedure of an early date and 2 FUT allergy). The mean duration of FUT for hemodialysis after gastric ESD was 11.5 ± 6.2 days. Bleeding after gastric ESD occurred in 6 (40.0%) of FUT group and 2 (66.7%) of LMWH group. Adverse events due to using FUT did not occur and no significant difference was shown about another complications excluding post-ESD bleeding between hemodialysis and non-hemodialysis patients. Patients characteristics and results:

| | Non-HD (n = 522) | HD (n = 18) | p value |
|---|---|---|---|
| Sex (male) | 422 (80.8%) | 14 (77.8%) | N.S. |
| Age (>=75years) | 320 (61.3%) | 15 (83.3%) | N.S. |
| Diameter (>=4.0 cm) | 32 (6.3%) | 0 (0.0%) | N.S. |
| Location | | | |
| -Upper third | 105 (20.2%) | 4 (22.2%) | N.S. |
| -Middle third | 161 (30.9%) | 3 (16.7%) | N.S. |
| -Lower third | 255 (48.9%) | 11 (61.1%) | N.S. |
| Diagnosis | | | |
| -Carcinoma | 465 (89.1%) | 16 (88.9%) | N.S. |
| -Adenoma | 44 (8.4%) | 2 (11.1%) | N.S. |

(continued)

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| | Non-HD (n = 522) | HD (n = 18) | p value |
|---|---|---|---|
| Ulcer | 18/464 (3.9%) | 2/16 (12.5%) | N.S. |
| Diabetes Mellitus | 113 (21.7%) | 9 (50.0%) | p = 0.01 |
| Hypertension | 246 (47.1%) | 11 (61.1%) | N.S. |
| Cerebrovascular disease | 21 (4.0%) | 3 (16.7%) | p = 0.04 |
| Cardiovascular disease | 101 (19.4%) | 8 (44.4%) | p = 0.02 |
| Liver cirrhosis | 13 (2.5%) | 0 (0.0%) | N.S. |
| Anti-platelet therapy | 109 (20.9%) | 10 (55.6%) | p = 0.002 |
| Dual anti-platelet therapy | 20 (3.8%) | 3 (16.7%) | p = 0.04 |
| Anti-coagulant therapy | 20 (3.8%) | 0 (0.0%) | N.S. |
| Complications | | | |
| -Bleeding | 38/519 (7.3%) | 8 (44.4%) | p < 0.0001 |
| -Perforation | 13/519 (2.5%) | 1 (5.6%) | N.S. |
| -Pneumonia | 3 (0.6%) | 0 (0.0%) | N.S. |
| -Stenosis | 2 (0.4%) | 0 (0.0%) | N.S. |

**Conclusion:** In hemodialysis patients, bleeding after gastric ESD occurred at a high rate in the use of FUT, as in the case with LMWH. We thought that it needed more cases to confirm the statistical efficacy of FUT as an anticoagulant for hemodialysis after gastric ESD to prevent post-ESD bleeding.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0143 FEASIBILITY OF A STRUCTURED INTERNATIONAL ESD TRAINING PROGRAMME FOR INTERNATIONAL DOCTORS IN JAPAN

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**Introduction:** Endoscopic submucosal dissection (ESD) is an important procedure which is minimally invasive, safe and provides excellent en-bloc resection of superficial mucosal tumour of the gastrointestinal tract. However, ESD experience and skill is still largely limited to Japan and a few countries in Asia.[1] Dissemination of such technique to the West has been difficult due to various reasons. This situation may potentially change, as the licensing law in Japan has changed to allow international medical doctors to pursue short-term clinical and endoscopic training under the supervision of a Japanese government certified expert without subjecting to Japanese licencing examinations. We have successfully initiated the first international ESD programme in Japan to allow an international doctor to work in our hospital under the supervision of an ESD expert.
**Aims & Methods:** The programme was initiated first by consultation with different ESD experts in Japan in terms of requirements prior to ESD training, diagnostic ability, hands-on training time, haemostasis skills and polypectomy skills required. Once a structured programme is established, a UK-trained gastroenterologist who is interested in learning ESD was then invited by our hospital. The training duration is dictated by our international trainee and the programme is then modified. First step in the application was approval by the Japanese Ministry of Justice for entry clearance. After this, application to the Ministry of Health for a provisional licence to practice in 'advanced clinical training' is required. Upon clearing the necessary documents for entry and practice, the trainee must purchase Japanese indemnity insurance for the time duration of the training. There was no funding for the programme and the international trainee is required to prepare his/her own expense for the duration of training in Japan. The structured training programme was then commenced.
**Results:** The duration of our programme was only for 3 months, as this was the duration our international trainee could afford. The programme commenced with 2 weeks of narrow band imaging (NBI) diagnostic training. If an ESD case is done, the trainee is required to observe and at times begin with the assistant role in ESD. After a total of 4 weeks into observing, being an assistant and continual NBI training, the trainee is allowed to perform under supervision, part of submucosal dissections during the procedure. Into the second month, the trainee continues to either observe ESD being performed and also performs part of the procedure. Learning content for the second month involved placing markings, initial dissections with the Dual Knife and haemostasis technique during ESD. Into the third month, ESD learning is expanded into learning about spatial importance of using gravity during ESD, depth recognition to avoid perforation and further intraoperative haemostasis techniques. During the third month the trainee also has the opportunity to visit the National cancer centre, Tokyo and St Luke's international hospital to observe ESD being done by other expert Japanese centres. The advantages of this programme gained from the trainee's perspective was a step by step learning of ESD under direct supervision, opportunity to observe expert ESD cases, learning from peers and international connections. Areas that may disadvantage the programme from the trainee's perspective may include lesser time dedicated to training of the international trainee due to local trainee also training in ESD, lack of cases at times and difficulty with communication sometimes. These were however, issues that can be addressed and improved.
**Conclusion:** We describe the first international ESD training programme set up in Japan for international trainees. As this is the index case in Japan, we have also gained valuable experience in training and teaching for the potential international trainee. In the future, we hope to design a further improved international ESD training programme in collaboration with the Japanese Ministry of Health and ESD experts in Japan.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0144 TREATMENT OUTCOMES OF ESOPHAGEAL SCC WITH MM INVASION COMPARING ENDSCOPIC RESECTION AND OPERATION

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**Introduction:** Recent advances in endoscopic resection (ER) provide us increasing chances for resecting esophageal SCC with muscularis mucosae (MM) invasion. As MM invasive cancer is reported to have 8–18% of metastatic risks and is defined as relative indication for ER in guideline by Japan Esophageal Society. For them, we perform additional therapy such as chemo radiotherapy (CRT) or operation considering the risk of metastasis and patients' condition. However, there is only a few reports of long term outcome of ER comparing to operation.
**Aims & Methods:** We retrospectively studied the long-term outcome in 143 cases of esophageal SCC with pathological MM invasion resected by ER (108 cases) and operation (35 cases) from 2003 to 2013 in Cancer Institute Hospital. Median observation period was 36 months for ER cases and 50 months for operation cases.
**Results:** Median age for ER and operation cases were 66 and 64. Median lesion size in ER cases were significantly smaller than that in operation cases (23 mm vs 44 mm, $P < 0.01$). Lymphovascular invasion were observed 7.1% in ER cases and 25.7% in operation cases. It was implicated that operation cases were more advanced cancer, although pathological depth of invasion were both MM. Of 108 cases of ER, 87 cases were observed without additional treatment. Two cases had recurrence as LN metastasis. One received operation and CRT and one received CRT, surviving with no re-recurrence. The rest of 21 cases were recommended additional therapy because of lymphovascular invasion or droplet infiltration and 12 cases were performed additional therapy (operation/CRT/RT 6/5/1). Seven cases had local recurrence after ER, however they were salvaged by re-ER or argon plasma coagulation. No one died of esophageal SCC. Of 35 cases of operation, two cases had recurrence including one LN metastasis and one lung metastasis. Both of two cases were died of esophageal SCC. Overall survival rate in 3 year/5 year were 87.8%/85.5% in ER cases and 89.7%/85.4% in operation cases. Cause specific survival rate in 3 year/5 year were 100%/100% in ER cases and 96.8%/96.8% in operation cases.
**Conclusion:** The long term outcome of ER for MM invasive esophageal SCC was very good with appropriate additional therapy. ER for MM invasive esophageal SCC is feasible.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0145 DISCRIMINATING FACTORS FOR SIGNIFICANT BLEEDING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION NEEDING EMERGENT HEMOSTASIS

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**Introduction:** It is hard to decide whether to perform emergent hemostasis or not, when gastric post-endoscopic submucosal dissection (ESD) bleeding occurs.
**Aims & Methods:** To clarify discriminating factors for significant gastric post-ESD bleeding needing emergent hemostasis. We retrospectively reviewed medical records of subjects who developed bleeding after ESD for gastric neoplasms between January 2005 and February 2011. Their comorbidities, biochemical results, pathologic characteristics, previous ESD history, current medication, and clinical findings at the time of bleeding events were reviewed. Significant bleeding was defined as bleeding which needed embolization or endoscopic hemostasis for visible exposed vessels or ongoing bleeding.
**Results:** Out of the total 2, 039 ESD patients, 309 had post-ESD bleeding. Among them 113 (36.6%) underwent endoscopy and 73 (23.6%) needed embolization or endoscopic hemostasis. Overall, hypoalbuminemia (OR 19.743, 95% CI: 2.084–187.011, p = 0.003), specimen size (OR 1.252, 95% CI: 1.025–1.528,

p = 0.027), and previous adjacent ESD history (OR 6517, 95% CI: 1.593–26.669, p = 0.009) were independently related with significant bleeding. Whereas, location of the lesion, malignant pathology, and shock at the time of bleeding event were not associated with significant bleeding.
**Conclusion:** For post-ESD bleeding in those with hypoalbuminemia, large specimen size, or previous adjacent ESD history, emergent hemostasis should be considered.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0146 DIAGNOSTIC ACCURACY OF ENDOSCOPIC FORCEPS BIOPSIES FOR SUPERFICIAL GASTROINTESTINAL LESIONS

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**Introduction:** The lack of diagnostic accuracy of endoscopic biopsies for superficial gastrointestinal lesions may inadequately select patients for surgery that could be treated by endoscopy and underestimate malignant lesions.
**Aims & Methods:** The authors aim to determine whether an adequate histological diagnosis of superficial gastrointestinal lesions can be attained on the basis of forceps biopsy and identify clinicopathological factors predicting reliability. Retrospective analysis of all gastrointestinal lesions treated by endoscopic submucosal dissection (ESD) in a Centre with previous histological assessment from forceps biopsies was done. Agreement between pre and post ESD histological assessment and clinicopathological factors predicting reliability (localization, tumor size and endoscopist profile) were evaluated.
**Results:** Of the 50 gastrointestinal lesions treated by ESD, 36 (6 esophageal, 22 gastric and 8 rectal) from 35 patients had previous histological evaluation from forceps biopsies. When biopsies results were compared, disagreement was found in 13 cases (36%), particularly high in rectal lesions (50%, n = 4), followed by gastric lesions (40%, n = 9). In the majority of them, forceps biopsies underestimated the final histological diagnosis (69%, n = 9) although overstaging was made in 3 cases (23%). From the analyzed clinicopathological factors, only endoscopist's ESD experience was associated with a higher agreement (p = 0.034, OR 10.83).
**Conclusion:** The disagreement between endoscopic forceps biopsies and post ESD specimen evaluation is high. Histological diagnosis from endoscopic forceps biopsies must be interpreted carefully and in the setting of a high-quality endoscopic evaluation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0147 THE USE OF ENDOCLOT AS HEMOSTATIC POWDER DURING GASTROINTESTINAL ENDOSCOPY

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**Introduction:** Gastrointestinal bleeding (GIB) can be due to a plethora of disease, such as ulcers and liver cirrhosis, or can occur as result of iatrogenic interventions. It is still a demanding indication for GI endoscopy with high morbidity and mortality rates; thus hemostatic powders such as EndoClot have been developed to improve endoscopic treatment.
**Aims & Methods:** In this study, we evaluated the application of EndoClot EndoClot Plus Inc., Santa Clara, CA, USA) during routine and emergency endoscopy over a one year period from consecutive unselected patients, arising from the real-life clinical day.
**Results:** EndoClot was applied during 25 endoscopies in 23 pts (1.08 applications/pt.; 10 male and 13 female; age 70.5 yrs, 28–90).
In 18 pts EndoClot was applied during upper GI endoscopy (81.8%) and in 5 pts during lower GI endoscopy (27.7%) with a total success rate of short-term hemostasis in 19/23 pts (82.6%).
The detailed analysis of the 18 pts with upper GIB showed that endoclot was applied for various therapeutic/prophylactic settings. Endoclot application was used for 1) ultimative emergency rescue treatment in 8/18 pts with a 100% success rate, 2) first line treatment modality before any other hemostasis technique in 4/18 pts resulting in 75% hemostasis, 3) recurrence prophylaxis after conventionally achieved endoscopic hemostasis in 4/18 pts with 75% success, and 4) primary prophylaxis of post-interventional bleeding in 2 pts avoiding bleeding in 1 (50% success).
At the lower GIT EndoClot resulted in at least short-term hemostasis in 4/5 pts (80%). Of note, over all locations endoclot induced hemostasis in 7/9 pts (77.7%) with impaired coagulation/anticoagulants. No major complications were noted, but 1/23 pts died (4.3%), unrelated to GIB.
**Conclusion:** EndoClot is a further and safe option for the treatment in GI endoscopy. It can be used as first line therapy (especially hampered coagulation), after failure of other hemostatic options or prophylactically after achieved hemostasis or interventions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0148 CLINICAL APPLICATION OF ENDOSCOPIC MINIMALLY INVASIVE THERAPEUTIC TECHNIQUES FOR UPPER GASTROINTESTINAL SUBMUCOSAL TUMORS

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**Introduction:** Little is known about the clinical outcomes among different endoscopic minimally invasive therapeutic techniques for upper gastrointestinal submucaosal tumors (SMT).
**Aims & Methods:** To evaluate the efficacy safety and clinical application value of endoscopic minimally invasive therapeutic techniques for upper gastrointestinal submucaosal tumors, 84 patients with upper gastrointestinal submucosal tumors (SMT) underwent endoscopic submucosal excavation (ESE), endoscopic submucosal dissection (ESD), submucosal tunneling endoscopic resection (STER) and endoscopic full-thickness resection (EFTR) after the examination of endoscopy, endoscopic uhrasonography and CT at Endoscopy Center, Department of Gastroenterology, the First Affiliated Hospital of Zhejiang Chinese Medical University from March 2013 to March 2015. There were 40 males and 44 females with an age range of (51.5 ± 9.3) years. The appearances of lesions and operative complications were recorded. The specimens were definited with pathological diagnosis, and postoperative therapeutic effect and safey were followed up.
**Results:** Of the 84 SMTs, 26 SMTs were located in esophagus, 6 in cardia, 23 in fundus, 10 in gastric body, 19 in gastric antrum. The results of EUS suggested that 52 SMTs were originating from muscularis propria layer (61.9%), 23 originating from mucosal muscular layer (27.4%)) 9 originating from submucosal layer (10.7%); The appearances of lesions were regular (n = 66) and irregular (n = 18). The overall rate of complete resection was 97.6% (82/84). Among them, the complete resection rate of ESD, ESE, STER and EFTR were 97.7%, 100%, 93.8% and 100%, with a mean diameter of (1.33 ± 0.61), (1.47 ± 1.12), (1.76 ± 0.98) and (1.36 ± 0.86) cm, a mean operative duration of (46 ± 29), (39 ± 16), (53 ± 23) and (44 ± 25) min, a mean hemostatic clips amount of (4.2 ± 1.8), (7.5 ± 2.8), (6.4 ± 2.1) and (7.8 ± 3.5). 3 cases occurred perforation during operation and 3 cases of subcutaneous emphysema, 3 cases of postoperative fever associated with elevated WBC, 3 cases of pneumoperitoneum and 2 cases of delayed bleeding were occurred after procedure. Of these patients, 1 case of delayed bleeding received surgical stomach resection and others were treated conservatively. The mean hospital stays after procedure were (5.98 ± 2.11) days (range 3–12 days). Among the 84 patients, 40 cases were pathologically proved to be leiomyoma (47.6%), 29 cases to be stromal tumor (34.5%), 8 cases to be ectopic pancreas tissue (9.5%), 3 cases to be lipoma (3.6%), 2 cases to be unknown pathological type of spindle cell tumor (2.4%), 1 case to be inflammatory polyp (1.2%) and 1 case to be submucosal cyst (1.2%). During a follow-up period of 1–18 months, no recurrence or residual lesions were noted in 67 patients (67/84, 79.8%).
**Conclusion:** Clinical application of endoscopic minimally invasive therapeutic techniques including ESD, ESE, STER and EFTR has proved to be safe and effective for upper gastrointestinal submucosal tumors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0149 INDIVIDUAL SKILLS PARAMETERS ASSOCIATED WITH COMPETENCY AT COLONOSCOPIC POLYPECTOMY: A RETROSPECTIVE ANALYSIS OF DIRECTLY OBSERVED POLYPECTOMY SKILLS (DOPYS)

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**Introduction:** The Directly Observed Polypectomy Skills (DOPyS) is a validated tool used to assess polypectomy skills in the United Kingdom. Polypectomy performed by a trainee is documented with DOPyS in an e-portfolio. DOPyS has 34 parameters of technical & non-technical skills (1) on which a trainee is scored on a grade of 1–4. Scores of 3 and 4 are accepted as being competent in a descriptor. Trainees are certified as competent in Level 1 (< 1 cm) & Level 2 (1–

2 cm) polypectomy if they achieve overall grades 3 or 4 for more than 90% of their last 4 consecutive DOPyS & a caecal intubation rate (CIR) >90% (over last 3 months). There is paucity of literature on the rate and type of skills acquisition required by trainees to achieve safe and competent polypectomy. Stable colonoscope position, tip control, CIR, variability in the endoscopists' technique & time spent to examine the polypectomy site have all been suggested as factors critical in effective polypectomy (2).

**Aims & Methods:** Retrospective data from the e-portfolio of 707 trainees (4965 DOPyS) from Jan 2009 to Sept 2015 was extracted. The low-scoring (grade 1 & 2) descriptors were identified and further analysed according to site, morphology and size of polyps removed. We also analysed a further subset of 61 trainees (749 DOPyS) & data were collected for absolute CIR at first recorded polypectomy assessment and at provisional/Full certification.

**Results:** 4965 DOPyS were analysed. 80% (3898) left sided polyps, 20% (976) right sided. 1851 (37%) stalked polyps, 3114 (63%) sessile polyps. Median size of the polyps was 6 mm & the majority (68%) <1 cm.

Trainees in UK scored grade 1 or 2 for the following parameters:

1) Preparation checks (non-technical skill): Checking for snare closure = 10% (411) & diathermy settings = 10% (474).

2) Technical skills: advancing snare sheath (8%), directing snare accurately (8%), positioning snare over the lesion (8%) and appropriate submucosal injection technique (8%) 3) Post polypectomy "Polyp retrieval" (4%).

Additionally, trainees were assessed as less competent for right-sided polyps vs left-sided polyps in skills such as choosing appropriate polypectomy technique (7%) and treating residual polyp (7%). The subset analysis of absolute CIR for 61 (749 DOPyS) trainees is shown in the table.

| | Median | n |
|---|---|---|
| **Number of lower GI procedures at first recorded DOPyS** | 137 (5-508) | 61 |
| **Absolute CIR at first recorded DOPyS (%)** | 73 (0-100) | 61 |
| **Absolute CIR at Level 1 polypectomy competency (%)** | 86 (47-94) | 42 |
| **Absolute CIR at Level 2 polypectomy competency (%)** | 88 (60-93) | 19 |

**Conclusion:** Trainees in the UK start formative assessment of polypectomy after completing >130 lower GI procedures with a CIR > 70%. Polypectomy competency in UK trainees is achieved with absolute CIR > 86%. This suggests that DOPyS competency increases with technical competence in colonoscopy and validates the assessment requirement of CIR > 90% over the last 3 months. We have identified several details of polypectomy technique (both technical & non–technical) that trainees are assessed as incompetent during the early phase of learning polypectomy, particularly for right sided polypectomy. Identification of these factors has potential to shorten the learning curve of polypectomy skills acquisition with targeted interventions like e-learning modules and specific in-vivo training.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0150 ACCURACY OF MODERN ENDOSCOPIC IMAGING TO DETERMINE THE KUDO NEOPLASTIC PIT PATTERN OF LARGE LATERALLY SPREADING COLONIC LESIONS (LSL)


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**Introduction:** Expert opinion suggests that the discrimination of pit pattern of colorectal lesions, first described by Kudo (Kudo neoplastic pit pattern, KPP), requires a chromic dye combined with magnification endoscopy. Endoscopic imaging has become so advanced that chromendoscopy may no longer be necessary for the discrimination of the KPP.

**Aims & Methods:** The study aimed to evaluate the diagnostic accuracy of high definition white light (HD-WL) and narrow-band imaging (NBI) for the discrimination of KPP to predict lesion histopathology without magnification or chromendoscopy. Amongst a prospective observational study of patients referred for WF-EMR of laterally spreading lesions (LSL) > 20 mm, successive lesions were analysed prior to resection for KPP using HDWL and NBI including the 'near focus' magnification mode where available. Olympus H180/HQ190 endoscopes were used throughout. 10 endoscopists, experienced in advanced endoscopy at fellow or consultant level interpreted the KPP. Lesion histopathology was determined later by two expert gastrointestinal histopathologists. KPP II, III + IV and V were correlated to sessile serrated adenoma, tubular adenoma/tubulovillous adenoma and invasive cancer respectively. Since the therapeutic approach for KPP III/IV is identical these were logically grouped together. The primary outcome was congruence of endoscopic pit pattern assessment with histology.

**Results:** From January 2015 to April 2016, 162 patients (mean age 68.4 years, 53.2% male) with 173 lesions (median size 35 mm (IQR 25–50 mm), 61.5% proximal colon) were referred for WF-EMR at a single tertiary referral endoscopy centre. Analysis of Kudo pit pattern was available for 169 lesions. Endoscopic assessment of the KPP was correct in 159/169 (94.1%) of cases. The endoscopic prediction of KPP II was correct in 12/15 lesions (accuracy 80%, 95% confidence interval 51.3–94.7%). KPP III or IV was correctly predicted in 146/152 cases (accuracy 96.1% – 95% confidence interval 91.2–98.3%). Where endoscopic imaging incorrectly predicted the KPP in this group (n = 6), 2/6 (33.3%) lesions were dysplastic serrated adenomas, known to exhibit areas of KPP III/IV. KPP V was only seen in 2 lesions, one was determined as invasive adenocarcinoma at histopathology, the other tubulovillous adenoma with diffuse high grade dysplasia. Key data regarding the endoscopic prediction of kudo neoplastic pattern is presented in table 1.

**Table 1:** Correct endoscopic assessment of Kudo neoplastic pit pattern (KPP) compared to histopathology; 95% CI – 95% confidence interval, SSA-ND – sessile serrated adenoma without dysplasia, SSA-D – SSA with dysplasia, TVA – tubulovillous adenoma, HGD – high grade dysplasia.

| **Kudo Neoplastic Pattern (KPP)** | Correct Endoscopic Assessment n = 169 | Accuracy (95% CI) | Histopathology where endoscopic assessment of KPP was incorrect n = 10 |
|---|---|---|---|
| II | 12/15 | 80% (51.3-94.7) | Tubular, 1 (33%) TVA, 2 (66%) |
| III/IV | 146/152 | **96.1% (91.2-98.3)** | SSA-ND, 3 (50%) SSA-D, 2 (33.3%) Invasive Cancer, 1 (16.7%) |
| V | 1/2* | | TVA HGD, 1 |

**Conclusion:** Kudo pit pattern can be reliably determined by advanced endoscopic imaging in the majority of cases, obviating the need for chromendoscopy. In particular, KPP III and IV, suggesting endoscopic resectability, were correctly predicted in over 95% of cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0151 THE CLINICAL SIGNIFICANCE OF SOLITARY LARGE SESSILE SERRATED ADENOMAS


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**Introduction:** Serrated lesions are a heterogeneous group of polyps with variable malignant potential. Although up to 30% of CRC develop via the serrated pathway, the natural history and malignant potential of solitary large (≥20 mm) SSAs (S-SSAs) is still incompletely understood.

**Aims & Methods:** To describe the characteristics of S-SSAs in comparison to large SSAs (≥20 mm) in patients with serrated polyposis syndrome (SPS) and unravel their clinical significance. Data was collected prospectively from a single tertiary referral center between September 2008 and July 2015. Patients with one or more large (≥20 mm) SSA were eligible. Data was collected from the diagnostic procedure performed by the referring endoscopist, the EMR procedure and the first surveillance colonoscopy (SC1). Based on these 3 procedures, patients were categorised in 3 groups: the S-SSA group, SPS group and the group of patients with ≥1 SSA without fulfilling the criteria of SPS (2-4 SSAs of which 1 is ≥20 mm). The SPS group was compared to the S-SSA group and the 2-4 SSAs group for patient and lesion characteristics and polyp burden.

**Results:** 151/1027 (14.7%) lesions removed by EMR were SSAs ≥20 mm. 30/151 (19.9%) lesions were excluded as they could not be assessed for polyp burden (18/30 did not undergo SC1 and 12/30 underwent surgery). 57/121 (47.1%) of patients had SPS, 43/121 (35.5%) had only 1 large SSA and 21/121 (17.4%) belonged in the 2-4 SSA group.

In the S-SSA group the lesion size was significantly smaller (25 vs 30 mm, p = .023), showed more submucosal fibrosis (23.3% vs 5.3%, p = .008) and was more frequently located proximal to the transverse colon (79.1% vs 57.9%, p = .026) as compared to the SPS group. In terms of polyp burden, patients with SPS had more conventional adenomas (14% vs 0%, p = .010) and more

high-risk adenomas (29.8% vs 9.3%, p = .014) than the S-SSA group. The presence of dysplasia was similar in both groups and relatively high (21% in the SPS group and 17% in the S-SSA group). There were no differences noted between the group with SPS and the 2-4 SSA group. In only 5/57 (10.9%) of cases, SPS was recognized by the referrer.

**Table 1:** Comparison between SPS and S-SSA and SPS and the 2-4 SSAs group. SPS: serrated polyposis syndrome; S-SSA: solitary large sessile serrated adenoma, SD: standard deviation; Hx: history; CRC: colorectal carcinoma; IQR: interquartile range; n/a: not applicable; high-risk adenoma: presence of an advanced adenoma or ≥3 adenomas.

| | SPS n = 57 | S-SSA n = 43 | P | 2-4 SSAs n = 21 | P |
|---|---|---|---|---|---|
| **Baseline characteristics** | | | | | |
| Age (mean; SD) | 64.6 (13.5) | 66.2 (11.4) | .547 | 64.8 (9.1) | .963 |
| Male (%) | 16 (35.1) | 18 (41.9) | .490 | 8 (38.1) | .806 |
| Personal Hx CRC (%) | 9 (15.8) | 4 (9.3) | .340 | 1 (4.8) | . 272 |
| Familial Hx CRC (%) | 11 (20.8) | 7 (16.7) | .614 | 4 (20.0) | 1.000 |
| Personal Hx polyps (%) | 51 (89.5%) | 38 (88.4) | .862 | 19 (90.5) | .942 |
| SPS recognised by referrer (%) | 5 (10.9) | n/a | | n/a | |
| **Lesion** | | | | | |
| Size (mm) (median, IQR) | 30 (25-40) | 25 (20-30) | **.023** | 30 (25-35) | .705 |
| Submucosal fibrosis (%) | 3 (5.3) | 10 (23.3) | **.008** | 4 (19.0) | .080 |
| **Location** | | | | | |
| Right colon (hepatic flexure and proximal) (%) | 33 (57.9) | 34 (79.1) | **.026** | 12 (57.1) | .952 |
| **Dysplasia** | | | | | |
| None (%) | 36 (63.2) | 26 (60.5) | .919 | 14 (66.7) | 1.000 |
| Low Grade (%) | 20 (35.1) | 16 (37.2) | 7 (33.3) | | |
| High Grade (%) | 1 (1.8) | 1 (2.3) | 0 | | |
| Cancer (%) | 0 | 0 | 0 | | |
| **Follow up** | | | | | |
| Recurrence at SC1 (%) | 3 (1.8) | 3 (7.0) | .312 | 1 (4.8) | .469 |
| **Polyp burden** | | | | | |
| **≥1 High-risk adenomas (%)** | 17 (29.8) | 4 (9.3) | **0.014** | 7 (33.3) | .787 |
| **≥10 Conventional adenomas (%)** | 8 (14.0) | 0 | **.010** | 1 (4.8) | .431 |

**Conclusion:** The clinical significance of S-SSAs is unknown. There is a different colonic distribution and a lower polyp burden in patients with a S-SSA as compared to SPS. However, striking commonalties such as age and sex distribution, suggest that SPS is not an evolutionary process. Also, high rates of dysplasia were noted in all 3 groups warranting adequate surveillance of patients with large SSA/Ps given the risk of synchronous advanced neoplasia. Finally, SPS is only in the minority of cases recognised by the referring physician. This is however of paramount importance since SSA/Ps with dysplasia are thought to be largely responsible for the relatively high prevalence of proximal interval cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0152 IMMEDIATE AND DELAYED BLEEDING AFTER COLD SNARE POLYPECTOMY: A PROSPECTIVE SINGLE-ARM TRIAL

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**Introduction:** Cold snare polypectomy (CSP), a promising polypectomy technique without electrocautery, is generally accepted as a less invasive procedure and has little risk of delayed bleeding for subcentimetric colorectal polyps. However, the frequency of immediate bleeding and delayed bleeding after CSP for subcentimetric colorectal polyps has thus far not been reported in a prospective large cohort.
**Aims & Methods:** We conducted a prospective, single-arm trial in a tertiary cancer center to investigate the frequency of immediate and delayed bleeding after CSP. Patients with subcentimetric colorectal polyps scheduled to undergo endoscopic polypectomy were enrolled. Patients who underwent polypectomy with electrocautery were excluded after enrollment. First, CSP was performed for the detected lesions, which were predicted to be neoplastic lesions, and the resected specimens were retrieved. When immediate bleeding occurred, endoscopic hemostasis was performed. The participants were scheduled to visit our hospital within 1 month after their colonoscopy to assess post-procedural complications such as bleeding. We defined immediate bleeding as evident bleeding requiring endoscopic hemostasis just after CSP (during examination). Delayed bleeding was defined as evident bleeding requiring endoscopic hemostasis after the completion of an examination. The study protocol was approved by the institutional review board of our hospital and registered in the Clinical Trial Registry (UMIN000010879).
**Results:** A total of 434 patients were assessed for study enrollment. 7 cases refused to participate and were excluded from the study enrollment. Therefore, 427 patients were enrolled by the participating colonoscopists. Since one patient claimed to withdraw from the study enrollment before the procedure, she was excluded after enrollment. Since 72 cases had polyps larger than 10 mm, pedunclated, or depressed lesion, they were excluded from the study protocol. Finally, a total of 1312 subcentimetric polyps in 354 patients (median age; 68 y.o. male/female; 271:83) were analyzed. We performed 1312 CSPs for subcentimetric lesions (median tumor size 4 mm; 947 polypoid and 364 flat). Immediate bleeding requiring endoscopic hemostasis occurred in 41 lesions (3.1%), but all were easily managed with endoscopic clipping. Delayed bleeding requiring endoscopic intervention occurred in 5 patients (1.4%; 95% confidence interval, 0.2%–2.6%), all of which were ooze-type bleeds also easily controlled by endoscopic clipping. We encountered no perforation or fatal adverse events.
**Conclusion:** The incidence of delayed bleeding after CSP, while not nonexistent, was remarkably low. CSP has the potential to become a standard endoscopic therapy for subcentimetric polyps.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0153 IMPACT OF LOW-VOLUME VERSUS STANDARD-VOLUME BOWEL PREPARATION ON PARTICIPATION IN PRIMARY SCREENING COLONOSCOPY: A RANDOMIZED HEALTH SERVICES STUDY

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**Introduction:** Participation in primary colonoscopy screening programs is unsatisfactory. Bowel preparation for colonoscopy is one of the key barriers to participation in screening. Low volume (LV) bowel preparation is better tolerated than standard volume (SV) bowel preparation. We hypothesized that offering LV bowel preparation will increase participation in screening colonoscopy (SC) without negative effect on bowel preparation quality.
**Aims & Methods:** This was a multicenter, randomized health services study performed within the organized Polish Colonoscopy Screening Program. Individuals aged 55–64 years who were invited for SC between March and April 2015 were randomly assigned in a 1:1 ratio to the LV bowel preparation group (0.3 L sodium picosulphate/magnesium citrate plus 2 L of water, Citrafleet®) or SV bowel preparation group (4 L polyethylene glycol, Fortrans®) and invited by invitation letter 6 week before SC then reminding letter in case of no response. Both bowel preparations were routinely administered in a split-dose regimen unless SC was scheduled for early morning hours. Bowel preparation medications were dispensed free of charge along with standardized instructions to all invitees who contacted screening centers and agreed to participate in screening. The primary outcome measure was participation rate in SC within 3 months from the date proposed in invitation letter. The secondary endpoints were compliance with the bowel preparation instructions, a quality of bowel preparation assessed with the Boston Bowel Preparation Scale (BBPS) and adenoma detection rate (ADR). The study was powered to detect 2% point difference in participation rates between study groups at a 0.05 significance level.
**Results:** Of the 13, 621 individuals invited for screening over the study period, 6, 811 were assigned to the LV group and 6, 810 to the SV group. There was no significant difference between the groups in participation rate in SC (15.8% LV vs. 14.7% SV, p = 0.067). 747/1199 (62.3%) in the LV group and 718/1154 (62.2%) in the SV group prepared using split-dose regimen. Bowel preparation was adequate (≥2 points in the BBPS in each colonic segment) significantly more often in the SV group compared to the LV group (86.3% and 78.5%, respectively; $p < 0.001$) despite the fact that more participants from the LV group complied with a full-dose of bowel preparation (98.6% and 96.9%, respectively, p = 0.05). Similarly, bowel preparation in the right colon was adequate significantly more often in the SV group compared to the LV group (91.0% and 84.2%, respectively; $p < 0.001$). There was no difference in the ADR between groups (30.4% LV vs. 29.4% SV, p = 0.60).
**Conclusion:** LV bowel preparation did not improve participation rate with screening colonoscopy compared to SV. Bowel preparation was adequate significantly more often in the SV group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0154 NBI ENDOSCOPIC CRITERIA- A USEFULL TOOL TO CHARACTERIZE COLONIC LESIONS IN CLINICAL PRACTICE

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**Introduction:** The characterization of colonic lesions by narrow band imaging (NBI) endoscopy provides the opportunity for endoscopists to adopt a proper therapeutic and surveillance strategy. We studied the applicability of NBI endoscopic criteria in current practice for the identification and differentiation of adenomas and serrated polyps.
**Aims & Methods:** A high-definition magnification endoscope with an NBI system and dual-focus optical imaging (Evis Exera III, Olympus) was used to perform endoscopic procedures. The Workgroup serrAted polypS and Polyposis (WASP) classification, which combines NICE criteria and the Hazewinkel criteria, was used for endoscopic diagnosis. Brown color, brown vessels, oval tubular or branched surface pattern were endoscopic criteria used to diagnose adenomas. Lesions exhibiting two of the following features: clouded surface, indistinctive border, irregular shape, or dark spot inside crypts, were diagnosed as sessile serrated adenomas/ polyps (SSA/Ps). Histology was used as the reference standard.
**Results:** A total number of 275 patients were prospectively assessed and 328 lesions have been detected: 155 hyperplastic polyps (HPs), 156 adenomas, 15 SSAs, and 2 invasive cancers. A high confidence diagnosis was made in 266 (81%) of polyps. We obtained 83.8 (95%CI: 66.2–94.5) sensitivity (Se), 96.7 (95%CI: 90.6–99.3) specificity (Sp), 89.6 (95%CI: 72.6–97.8) positive predictive value (PPV) and 94.6 (95%CI: 87.9–98.2) negative predictive value (NPV) for adenomas detection in diminutive polyps (<5 mm in size); 96.6 (95%CI: 88.4–99.5) Se, 95.4 (95%CI: 77.1–99.8) Sp, 98.3 (95%CI: 90.9–99.9) PPV, 91.3 (95%CI: 71.9–98.9) NPV in small polyps (6–9 mm), and 95.2 (95%CI: 83.8–99.4) Se, 91.6 (95%CI: 61.5–99.7) Sp, 97.5 (95%CI: 87.1–99.9) PPV, 84.6 (95%CI: 54.5–98.0) NPV in large polyps (>9 mm in size), when polyps were assessed with high confidence. Specific NBI endoscopic criteria for SSA/Ps according to WASP classification were identified in 9 lesions (6 lesions were assessed with high confidence, 3 with low confidence), and histologic confirmation of SSAs was obtained in 7 of these lesions. Seven lesions diagnosed as HPs on NBI endoscopy and one adenoma (2 high confidence diagnosis, 6 low confidence diagnosis) proved to be SSAs at histology. Overall, the endoscopic criteria yielded 46.6 (95%CI: 21.2–73.4) Se, 98.7 (95%CI: 95.5–99.8) Sp, 77.7 (95%CI: 39.9–97.1) PPV, and 95.2 (95%CI: 90.7–97.9) NPV for SSAs diagnosis.
**Conclusion:** Our study proved the utility of NBI endoscopic criteria in characterization of colonic lesions. The diagnostic performance was good in high confidence predictions of histology. The detection of specific features for SSA/Ps may represent a challenge during real-time examination (7 SSAs did not meet the endoscopic criteria, and were underestimated as HPs). The implementation of a standardized classification system in clinical practice, as well as an adequate training for the identification of endoscopic criteria with high level of confidence, are mandatory for an accurate optical diagnosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0155 KNIFE-ASSISTED RESECTION OF RIGHT-SIDED COLONIC POLYPS: THE RIGHT WAY ROUND!

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**Introduction:** Endoscopic resection of right-sided colonic polyps carries an inherently higher risk of complications including bleeding and perforation. This risk is heightened in the resection of polyps that are tethered, flat or on background of colitis (complex polyps). In the West, complex polyps in the right colon are frequently managed by endoscopic mucosal resection (EMR) or surgery although recurrence rates can be as high as 20%. Endoscopic submucosal dissection (ESD) is an effective technique in the resection of complex polyps. However, ESD is technically challenging with a long learning curve and carries a significant perforation rate (6% in Eastern series and 17% in Western series) leading to a poor uptake of this technique in the West.[i], [ii].
**Aims & Methods:** We aim to examine the safety and efficacy of a novel technique of knife-assisted snare resection (KAR) in resecting complex polyps in the right colon. Data of all KARs undertaken at our institution from 2009 to 2015 were prospectively compiled in a pre-designed database. Independent researchers blinded to the technique interrogated this database. Polyps in the right colon (distal transverse to caecum) were included in the analysis. Polyp characteristics and procedure details were prospectively recorded. Endoscopic follow-up was performed to identify recurrence.
**Results:** A total of 52 patients with complex polyps 10–80 mm in size were resected by KAR. The mean follow-up time was 35 months. 42% of the polyps were >40 mm in size, and 51% were scarred from previous attempts. The majority of the polyps resected (91%) exhibited flat morphology (Paris Classification IIa, IIa + IIb, IIa + IIc). Table 1 shows the patient baseline and lesion characteristics. There were 2 cases of delayed bleeding (4%) neither of which required surgery. The endoscopic cure rate was 96% after single procedure, improving to 98% with further attempts.

**Table 1:** Patient baseline and lesion characteristics.

| | |
|---|---|
| Age, Years (Mean) | 46-83, (70) |
| Sex (M:F) | 2.7:1 |
| Mean polyp size, mm (range) | 35 (7-80) |
| En Bloc Resection, n (%) | 24 (45%) |
| Histology, n Adenoma SSP DALM Cancer | 36 12 3 4 |

**Conclusion:** This is the first reported Western series of KAR of complex polyps in the right colon. Although the en-bloc resection rate was low, our data demonstrates that this novel technique is a safe and effective technique for resection of complex polyps in the right colon. The recurrence rates are superior to EMR and complication rates are lower than ESD. As the learning curve for KAR is shorter than that for ESD, we believe that this technique is ideal for the Western setting.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0156 EFFICACY OF SMALL AND LARGE VOLUME PREPARATIONS AS FREELY CHOSEN BY PATIENTS TO OBTAIN A CLEAN COLON: ROLE OF VOLUMES, TIME DISTRIBUTION, DEMOGRAPHIC AND CLINICAL PARAMETERS IN A PROSPECTIVE, OBSERVER-BLINDED OBSVERVATIONAL STUDY

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**Introduction:** An adequate bowel preparation is an essential prerequisite for quality colonoscopy[1]. The identification of a patient's risk factors for inadequate colon cleansing and efficacy of preparation may result in the identification of personalized bowel preparation with positive impacts on both quality colonoscopy and patients' satisfaction.
**Aims & Methods:** This study was aimed at evaluating the efficacy of bowel cleansing preparation of a low-volume mixed preparation (20 mg bisacodyl plus 2 L polyethylene glycol solution with citrate and simethicone [PEG-CS + B], LOVOL-S) and a high-volume preparation (4 L polyethylene glycol solution plus simethicone [PEG-S], SELG-S) and the risk factors for inadequate cleansing in patients who were free to choose among the two types of preparations. This single-center, observer-blinded, observational trial enrolled all consecutive adult outpatients referred for colonoscopy. All subjects received a questionnaire asking on demographics (age, sex, body mass index [BMI]), clinics (Bristol stool chart, comorbidities, colonoscopy indication) and type of bowel preparation used. Patients were asked to freely choose between 4 L PEG-S one-day (subgroup A) or 2 L PEG-CS + B one-day dose (subgroup B) for morning colonoscopy, and 4 L PEG-S split-dose (subgroup C) or2 L PEG-CS plus 20 mg bisacodyl split-dose for afternoon colonoscopy. All colonoscopies were performed by experienced endoscopists (>300 colonoscopies/year), well-trained in the use of bowel preparation rating scales. Data concerning cecal intubation, Boston bowel preparation scale (BBPS) [2], Ottawa scale (OS) [2] were collected by the endoscopist, who was blinded to patient's data. The OS and BBPS scales were used as end points: a score ≤2 for each bowel segment was used as satisfactory for OS, while a score ≥2 for BBPS. Logistic regression was adjusted for sex, colonoscopy indication, Bristol stool chart, BMI, age, and number of

comorbidities in order to evaluate the association between the two bowel-cleansing preparations and the study end-points.
**Results:** Between December 2014 and March 2016, 1174 patients were enrolled; 100 of them were excluded for missing information in the questionnaire. In the remaining population, 51% were men, the mean age was 61 ys, the mean BMI 25 kg/m$^2$. 283 patients were allocated In subgroup A, 340 in subgroup B, 263 in subgroup C and 188 in subgroup D. Indications for colonoscopy were abdominal pain (10%); diarrohea (6%); constipation (6%); irregular bowel movements (3%); screening, also including post-polypectomy surveillance, proctorrhagia and anaemia (54%); inflammatory bowel disorders (9%); previous bowel surgical resection (7%); others (5%). Subgroups A-D showed an equal distribution of indications, age, sex, BMI and number of comorbidities.Data regarding the adequacy of bowel preparations are reported in the table below (table 1a). The odds of bowel cleansing observed with split regimens (either PEG-CS + B or PEG-S 4 L) are remarkably greater compared to the odds of the corresponding one-day regimens, regardless of the rating scale used, while no significant difference was observed between small or large volume preparations. Old age was the only variable significantly associated with inadequate bowel cleansing as assessed by either BBPS or OS (table 1b-f), while a trend was observed for BMI $\geq$ 30 for low BBPS.
**Conclusion:** This study confirms the efficacy of split-dose regimens with either low or high volume preparations for bowel cleansing. In patients free to choose among different preparations and regimens, we observed no relevant impact on cleansing. Our results confirm the risk of inadequate bowel cleansing in elderly and show some risk in obese subjects as well.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0157 IMPACT OF FULL SPECTRUM ENDOSCOPY (FUSE® ENDOCHOICE®) IN ADENOMAS DETECTION: FIRST FRENCH PROSPECTIVE STUDY


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**Introduction:** Colorectal cancer remains to this day a major public health problem. Currently, colonoscopy and polypectomy are the gold standard to prevent incident cases of colorectal cancer. This endoscopic examination can detect lesions at a curable stage and resect adenomas. Colonoscopy quality indicators have been defined by professional societies based on published studies. One of the most important is adenoma detection rate (ADR). American Society of Gastrointestinal Endoscopy (ASGE) recommend ADR of 20% or higher for female patients and 30% or high for male patients. Use of a new colonoscope with larger panoramic view up to 330° improve adenomas rate of 41% with 15% of advanced adenomas, in a tandem randomized multicenter study. Fuse® colonoscope system use three independent 170° imagers, one central and 2 laterals, each one being separately displayed on the screen. We wanted to confirm these results by producing the first French prospective observational study concerning the colonoscopy FUSE©.
The primary endpoint was potentially omitted adenomas (POA) i.e. adenomas seen on the side screens and will not appear on the central display during colonoscopy withdrawal without oriented movements. Secondary endpoints included our ADR team, FUSE© impact on ADR, time to cecal intubation and withdrawal time.
**Aims & Methods:** We did a monocentric prospective study in one french center (Paoli-Calmettes institute, Marseille, France). We enrolled patients aged over 18 years between January 2015 and March 2016 who had been referred for complete colonoscopy. We excluded individuals with a history of colonic resection, individuals with APC or MYH mutation, patients referred to endoscopic mucosal resection or endoscopic submucosal resection of a large adenoma and patients with bad bowel preparation. Informed consent was obtained from all participants.
**Results:** We included 141 patients between January 2015 and March 2016. Three patients were excluded of the final analysis on account of incomplete colonoscopies. The final analysis concerned 138 patients. Our study interested 78 men and 43 women (sex ratio = 1, 3). Mean age was 60.4 years. 130 polyps were resected without complication. Among these polyps, 88/130 were adenomas (68%). 3 CCR were found. Pathology of all adenomas was low grade dysplasia. Number of POA was estimated at 34. Therefore 34/88 adenomas (39%) were POA. Mean time to caecum was 10 minutes and mean withdrawal time was 12 minutes. 91 colonoscopies (66%) were performed by fellow under senior supervision and 34% only by senior. Global ADR was 34%. Men ADR was 35% and women ADR 31%. Estimated ADR without POA was 29% for men and 19% for women.
**Conclusion:** The results of our study support the use of FUSE© system for several reasons. First and foremost POA represented 39% of all adenomas and this

**Abstract: P0156: Table 1.**

| a - Adequacy of preparation score | Total | LovolEsse 2 L + LovolDyl 4cp one-day | LovolEsse 2 L + LovolDyl 4cp split | SelgEsse 4 L one-day | SelgEsse 4 L split |
|---|---|---|---|---|---|
| Boston Score >=2 for each segments | 972 (92.0) | 294 (87.7) | 175 (96.2) | 256 (91.8) | 247(95.7) |
| Ottawa Score <= 2 for each segments | 923 (87.5) | 265 (78.4) | 172 (95.0) | 239 (85.9) | 247 (95.7) |
| Ottawa Score <= 6 | 700 (66.4) | 182 (53.4) | 136 (75.1) | 179 (64.4) | 203 (78.7) |
| Boston Score right colon >=2 | 985 (93.1) | 299 (88.5) | 178 (97.8) | 259 (92.2) | 249 (96.5) |
| Ottawa Score right colon <= 2 | 936 (88.5) | 272 (80.5) | 177 (97.3) | 240 (85.7) | 247(95.7) |
| **b - Univariate and multivariable logistic regression models for Boston Score (cut off >=2 for each segments)** | | Univariate | Multiple | | |
| Risk category | OR (95% CI) | p-value | OR (95% CI) | p-value | |
| **Bowel preparation** | | | 0.0003 | | 0.001 |
| LovolEsse 2 L + LovolDyl 4cp split | LovolEsse 2 L + LovolDyl 4cp one-day | 3.74 (1.65-8.49) | 1.83 (1.02-3.29) | 3.68(1.59-8.50) | |
| SelgEsse 4 L one-day | 1.67 (0.98-2.83) | | 3.06(1.51-6.21) | | |
| SelgEsse 4 L split | 3.36 (1.69-6.65) | | 0.020 | | 0.063 |
| **BMI** | | 2.39 (1.30-4.40) | | 2.17(1.13-4.17) | |
| <25 | >=30 | 1.77 (0.95-3.31) | | 1.83(0.95-3.53) | |
| [25-30) | | 0.97 (0.95–0.99) | 0.0007 | 0.96 (0.94–0.98) | 0.0002 |
| **Age** | | Univariate | Multiple | | |
| **c - Univariate and multivariable logistic regression models for** | | | | | |

(continued)

**Abstract: P0156: Table 1.**. Continued

| a - Adequacy of preparation score | Total | LovolEsse 2 L + LovolDyl 4cp one-day | LovolEsse 2 L + LovolDyl 4cp split | SelgEsse 4 L one-day | SelgEsse 4 L split |
|---|---|---|---|---|---|
| **Ottawa Score (cut off <= 2 for each segments)** | | | | | |
| Risk category | OR (95% CI) | p-value | OR (95% CI) | p-value | |
| **Bowel preparation** | | | <0.0001 | | <0.0001 |
| LovolEsse 2 L + LovolDyl 4cp split | LovolEsse 2 L + LovolDyl 4cp one-day | 5.26 (2.57-10.80) | | 5.30(2.54-11.02) | |
| SelgEsse 4 L one-day | 1.69 (1.10-2.59) | | 1.82(1.14-2.91) | | |
| SelgEsse 4 L split | 6.19 (3.21-11.93) | | 6.65(3.30-13.38) | | |
| **BMI** | | | 0.069 | | 0.101 |
| <25 | >=30 | 1.85 (1.09-3.12) | | 1.83(1.03-3.24) | |
| [25-30) | | 1.59 (0.92-2.73) | | 1.75(0.70-3.14) | |
| **Age** | | 0.97 (0.96–0.99) | 0.0008 | 0.97 (0.95–0.98) | 0.0003 |
| **d - Univariate and multivariable logistic regression models for Ottawa Score (cut off <= 6)** | | Univariate | Multiple | | |
| Risk category | OR (95% CI) | p-value | OR (95% CI) | p-value | |
| **Bowel preparation** | | | <0.0001 | | <0.0001 |
| LovolEsse 2 L + LovolDyl 4cp split | LovolEsse 2 L + LovolDyl 4cp one-day | 2.59 (1.74-3.86) | | 2.85(1.86-4.39) | |
| SelgEsse 4 L one-day | 1.55 (1.12-2.15) | | 1.74(1.21-2.51) | | |
| SelgEsse 4 L split | 3.16 (2.19-4.57) | | 3.44(2.31-5.13) | | |
| **BMI** | | | 0.0004 | | 0.0009 |
| <25 | | 2.16(1.45-3.21) | | 2.28(1.48-3.52) | |
| [25-30) | >=30 | 1.56 (1.04-2.35) | | 1.77(1.13-2.75) | |
| **Age** | | 0.98 (0.97–0.99) | <0.0001 | 0.98 (0.97–0.99) | <0.0001 |
| **e - Univariate and multivariable logistic regression models for right colon Ottawa Score (cut off <= 2)** | | Univariate | Multiple | | |
| Risk category | OR (95% CI) | p-value | OR (95% CI) | p-value | |
| **Bowel preparation** | | | <0.0001 | | <0.0001 |
| LovolEsse 2 L + LovolDyl 4cp split | LovolEsse 2 L + LovolDyl 4cp one-day | 8.59 (3.39-21.74) | | 8.81(3.44-22.54) | |
| SelgEsse 4 L one-day | 1.46 (0.95-2.24) | | 1.60(1.00-2.54) | | |
| SelgEsse 4 L split | 5.45 (2.81-10.55) | | 5.88(2.91-11.86) | | |
| **BMI** | | | 0.033 | | 0.045 |
| <25 | >=30 | 2.02 (1.19-3.42) | | 2.03(1.14-3.62) | |
| [25-30) | | 1.73 (0.99-2.99) | | 1.90(1.05-3.46) | |
| **Age** | | 0.98 (0.97–0.99) | 0.004 | 0.97 (0.96–0.99) | 0.0018 |
| **f - Univariate and multivariable logistic regression models for right colon Boston Score (cut off >=2)** | | Univariate | Multiple | | |
| Risk category | OR (95% CI) | p-value | OR (95% CI) | p-value | |
| **Bowel preparation** | | | 0.0002 | | 0.0004 |
| LovolEsse 2 L + LovolDyl 4cp split | LovolEsse 2 L + LovolDyl 4cp one-day | 5.80 (2.04-16.51) | | 5.89(2.04-17.04) | |
| SelgEsse 4 L one-day | 1.54 (0.89-2.66) | | 1.71 (0.95-3.09) | | |
| SelgEsse 4 L split | 3.61 (1.72-7.59) | | 3.48(1.61-7.51) | | |
| **BMI** | | | 0.0064 | | 0.017 |

(continued)

**Abstract: P0156: Table 1.**. Continued

| a - Adequacy of preparation score | Total | LovolEsse 2 L + LovolDyl 4cp one-day | LovolEsse 2 L + LovolDyl 4cp split | SelgEsse 4 L one-day | SelgEsse 4 L split |
|---|---|---|---|---|---|
| <25 | >=30 | 2.69 (1.44-5.02) | | 2.46(1.26-4.79) | |
| [25-30) | | 2.22(1.16-4.24) | | 2.38(1.20-4.73) | |
| **Age** | | 0.97 (0.95–0.99) | 0.0016 | 0.97 (0.95–0.99) | 0.0019 |
| Multivariable models were adjusted for sex, indication of colonoscopy, bristol stool scale, cecal intubation, comorbidities, age and BMI, which resulted significant in univariate analisys. | | | | | |

confirms our primary endpoint. Achievement time of FUSE© colonoscopy was acceptable all the more so a lot (66%) of endoscopies was performed by fellow under senior supervision. Female ADR is congruent with ASGE guidelines since it is higher than 30%. Women ADR is also in agreement with ASGE guidelines. Impact of panoramic view on ADR was considered significant given that 10% increase of either sex. After several months of use of the FUSE© colonoscope, we think that FUSE© colonoscopy is feasible and reliable. This new scope improves the vision of the colonic lumen and may reduce the rate of interval cancers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0158 A PREDICTION SCORE TO IDENTIFY PATIENTS AT RISK FOR INADEQUATE BOWEL PREPARATION EVALUATED BY A SELF-ADMINISTERED QUESTIONNAIRE

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**Introduction:** Colonoscopy is the gold standard for colorectal cancer screening in general population. Adequate bowel preparation is important for optimal colonoscopy. The occurrence of interval cancers raises the problem of missed lesions. The rate of poorly prepared colonoscopies is established about 20 to 40%. This problem generates significant additional costs associated with colonoscopies redone, estimated at 35 million euros in 2008. It is important to identify patients at high risk of inadequate bowel preparation in this specific group.
**Aims & Methods:** To develop a prediction score to identify patients at high risk for inadequate bowel preparation evaluated by a self-administered questionnaire completed by patients during the pre - colonoscopy consultation. Main Outcome Measurements: Inadequate bowel preparation defined as Boston Bowel Preparation Scale. We performed a prospective study of 599 consecutive patients who underwent colonoscopy, from February to November 2015 at the University Hospital of Angers (France). Multivariate analysis was performed to identify factors associated with inadequate preparation, which were expressed as odds ratio (OR) and used to build a predictive model.
**Results:** A total of 599 colonoscopies were included, of which 24.5% (n = 147) had an inadequate bowel preparation (Boston Preparation score < 7). Mean age was 57.1 ± 14.3 years, 331 (55.3%) were male and indications for colonoscopy were screening and/or surveillance 320 (53.5%), abdominal symptoms and/ or blood loss and/or anemia 151 (25.3%), inflammatory bowel disease 65 (10.9%), and others (62 (10.4%), independent factors included in the prediction model were American Society of Anesthesiologists Physical Status Classification System score: ASA = 2 (OR = 1.57 [0.94–2.61]) and ASA > 3 (OR = 5.79 [3.12–10.77]), history of inadequate bowel preparation (OR = 3.86 [1.83–8.12]), and older age < 50 ans (OR = 2.89 [1.43–5.83]), older age between 50 et 70 ans (OR = 2.05 [1.12–3.75]). These factors predicted which patients would have inadequate cleansing with sensitivity 44.6 [42.8–46.4], specificity 81.1 [80.3–81.9], positive predictive value = 44.0, and negative pre- dictive value = 81.5; they had an under the receiver operating charac- teristic curve value of 0.671.
**Conclusion:** the use of this predictive score would allow the selective optimization of bowel preparation at the initial consultation to increase the percentage of colonoscopies properly prepared, and then reduce the number and the cost of rescheduled exams and the risk of interval cancers.
**Disclosure of Interest:** A. Berger: Norgine.
All other authors have declared no conflicts of interest.

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## P0159 EFFECTIVENESS OF ENDOSCOPIC SUBMUCOSAL DISSECTION USING THE "CLIP-FLAP METHOD" FOR SUPERFICIAL COLORECTAL TUMORS

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**Introduction:** Endoscopic submucosal dissection (ESD) is technically challenging because of poor visualization and instability in the operative field. Although mucosal flap formation improves visualization of the cutting area, it is difficult to achieve, especially in colorectal ESD. To facilitate mucosal flap creation, we developed the "clip-flap method" using the endoclip as a substitute for the mucosal flap until the flap is completed (K. Yamamoto, et al. Endoscopy 20122015).
**Aims & Methods:** We retrospectively studied 407 cases, in which ESD for superficial colorectal tumors was performed between August 2008 and April 2016. The primary object lesions were laterally spreading tumor, which were suspected to be intramucoal or with slightly invaded submucosal cancers > 20 mm in diameter in the operative examinations. We compared the treatment outcomes after the adoption of the clip-flap method (Clipflap-ESD: 287 cases) with those before the adoption of the clip-flap method (Conventional-ESD: 120 cases) to evaluate the efficacy and safety of the clip-flap method. The procedure of the clip-flap method is as follows. The lesions were moved upward as far as possible against gravity following a postural change to take advantage of the counter-traction of gravity. After submucosal injection, the mucosa around the lesion on the anal side was incised with an adequate margin, and the submucosal layer was cut deeply. The edge of the exfoliated mucosa was clipped with an endoclip (EZ CLIP, HX-610-135; Olympus). The distal attachment was inserted under the endoclip, and then the submucosal layer was dissected with the endoknife. A single endoclip was generally used, and the cross pattern of endoclips, created by attaching one endoclip to another endoclip, was also used according to the situations. We predominantly used a short-needle electrosurgical endoknife with a water-jet function (FlushKnifeBT; Fujifilm), and also used other endoknives in some cases.
**Results:** Median tumor diameter, resected specimen diameter, procedure time, en bloc resection rate, and perforation rate of Conventional-ESD and Clipflap-ESD were 26 mm vs 29 mm, 32.5 mm vs 36 mm, 88.5 minutes vs 59 minutes, 90% vs 97.2%, and 4.2% vs 1.4%, respectively. The procedure time of Clipflap-ESD was statistically significantly shorter than that of Conventional-ESD ($P < 0.01$), and en bloc resection rate of Clipflap-ESD was significantly higher than that of Conventional-ESD ($P < 0.01$). In all the cases which the clip-flap method was applied, the exfoliated mucosa was lifted by the endoclip attached to the exfoliated mucosa after the distal attachment was inserted under the endoclip, allowing for clear visualization and efficient dissection of the submucosal layer, and effective creation of the mucosal flap. The clip-flap method was effective even when it was difficult to insert the distal attachment under the exfoliated mucosa due to submucosal fibrosis or vertical approach. Perforation was conservatively treated with clipping in 8 of 9 cases. In only one case of C-ESD, laparotomy was needed due to difficult situation to repair, which was caused by poor visualization of cutting area.
**Conclusion:** The clip-flap method facilitated the mucosal flap creation and allowed our treatment outcomes to be dramatically improved. The present study demonstrates that the clip-flap method is a simple, safe, and very effective option for colorectal ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0160 ENDOSCOPIC SUBMUCOSAL DISSECTION IN A WESTERN SETTING: RESULTS AND LEARNING CURVE PROGRESS FROM A PROSPECTIVE SERIES OF 118 CASES IN TWO CENTERS

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**Introduction:** Endoscopic submucosal dissection (ESD) is an ideal advanced endoscopic technique for management of selected early gastrointestinal neoplasms (EGN) with low risk of lymph node involvement. Learning curve in Western setting is demanding, in particular for colorectal cases.
**Aims & Methods:** To assess therapeutic outcomes of ESD initiated in two tertiary centers in Madrid, we conducted a prospective evaluation of patients with EGN eligible for ESD. Prior intensive training program in animal model was completed by main operator (AH) from 2010 to 2012 (over 100 ESD cases completed). Clinical ESD procedures were mostly performed with Flush knife BT (Fujifilm Co.) and/or Hook knife (Olympus Co.), with 96% of patients under general anesthesia. We performed a global analysis and also time-framed analysis of the series to evaluate the ESD learning curve process, specifically assessing initial success, en-bloc & R0 resection rate, speed and complication rate.
**Results:** ESD was attempted in 118 lesions from January 2012 to April 2016. Majority of procedures were performed at Puerta de Hierro University Hospital (110/93.2%). Mean age was 65.8 years, with male proportion 58.5%. Most of the cases were colorectal (72%), with lower proportion of gastric (17.8%) and esophageal EGNs (10.2%). Initial success was achieved in 112 cases (95%), with en-bloc and R0 resection rate of 95% and 82.2% respectively. Mean lesion size was 30.5 mm (range 5–80), with median time to complete procedure 94.5 min (range 8–260). Perforation was the main complication, with a global rate of 34.7%, along with 5 cases (12.2%) requiring early surgical management. Late complications were identified in 11 patients: delayed perforation (4), bleeding (3), electrocoagulation syndrome (1), severe esophageal stricture (1), haemoperitoneum (1) and splenic rupture (1). All but 4 cases (36%) were successfully managed with medical and/or endoscopic treatment. The mean hospital stay for patients without complications was 2.5 (SD 2.1) days. Results from the learning curve progression according to 4 consecutive chronological blocs of 30 cases are summarized in table 1. Initial success increased from 86.7% to 100%, along with similar rise of en-bloc resection rate. An increasing proportion of colorectal cases up to 82–83% on the 2 final periods were noticed. Speed of ESD increased after the first 30 cases (0.14 $cm^2$/min), with a plateau of 0.22–0.26 $cm^2$/min subsequently. A high perforation rate in the first period (43%) was noteworthy, with a slight reduction to 30–35% on the following periods. It was remarkable that endoscopic treatment was successful in all cases of perforation along the final period analyzed.
**Conclusion:** High rates of success and en-bloc resection can be achieved after intensive training and learning curve progress on ESD, even in a high prevalence-based approach of colorectal EGN. Perforation in such realistic environment is still a challenge for Western endoscopists. Nevertheless, increasing experience reflects in a remarkable success in endoscopic management of perforation, which eventually can help to overcome such constrain.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0161 EXPECTED DIAGNOSTIC PERFORMANCE OF JOINT USE OF FECAL IMMUNOCHEMICAL TEST AND FLEXIBLE SIGMOIDOSCOPY IN COLORECTAL CANCER SCREENING

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**Introduction:** Fecal immunochemical tests (FITs) and flexible sigmoidoscopy (FS) are less invasive alternatives to colonoscopy in colorectal cancer (CRC) screening. FITs detect the majority of CRCs but have limited sensitivity to detect advanced adenomas (AA). FS detects neoplasms in the left colon and rectum only.
**Aims & Methods:** We aimed at assessing the expected diagnostic performance of combined use of FIT and FS. We systematically reviewed screening studies conducted in an average risk population that reported specificities and site-specific sensitivities of FITs for detection of CRC or AA. PubMed and Web of Science were searched until September 4th, 2015. Reference lists of eligible studies were also screened. Sensitivity of FS was derived from colonoscopy results, assuming

**Abstract No: P0161: Table 1**

| N = 118 | 1-30 | 31-60 | 61-90 | 91-118 | Total (n/%) |
|---|---|---|---|---|---|
| Colorectal location | 19/30 (63.3%) | 18/30 (60%) | 25/30 (83.3%) | 23/28 (82.1%) | 85/118 (72%) |
| Success | 26(86.7%) | 29 (96.7%) | 29 (96.7%) | 28 (100%) | 112 (95%) |
| En bloc | 26(86.7%) | 29(96.7%) | 29 (96.7%) | 28 (100%) | 112 (95%) |
| R0 | 24 (80%) | 27 (90%) | 24 (80%) | 22(78.6%) | 97(82.2%) |
| Speed(cm2/min).Mean (SD) | 0.14 (0.06) | 0.23 (0.17) | 0.26(0.18) | 0.22(0.15) | 0.21(0.15) |
| Perforation | 13 (43.3%) | 9 (30%) | 9 (30%) | 10(35.7%) | 41(34.7%) |
| Surgery | 2/13(15.4%) | 2/9(22.2%) | 1/9(11.1%) | 0/10 (0%) | 5 (12.2%) |

0% sensitivity for right- and 100% sensitivity for left-sided neoplasms. Bivariate meta-analyses across studies were used to derive summary estimates of overall sensitivity and specificity of individual and joint application of both tests.
**Results:** Ten eligible studies were identified. Summary estimates (95% CI) of overall sensitivity for detecting CRC and AA were 64% (56–72%) and 26% (21–32%) for FIT alone, 61% (51–70%) and 59% (48–69%) for FS alone, and 86% (80–90%) and 68% (60–76%), respectively, for the combination of both tests. The pooled specificity (95% CI) of FIT alone or in combination with FS was 93% (90– 95%).
**Conclusion:** Combined use of FS and FIT would detect close to 90% of CRCs and two out of three AAs at a high specificity.
**Disclosure of Interest:** T. Niedermaier: Research on CRC screening conducted in the Division of Clinical Epidemiology and Aging Research, DKFZ, has been or is currently being partly funded by industrial research grants from Eiken Chemicals, Epigenomics, Roche Diagnostics and Applied Proteomics.
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H. Brenner: Research on CRC screening conducted in the Division of Clinical Epidemiology and Aging Research, DKFZ, has been or is currently being partly funded by industrial research grants from Eiken Chemicals, Epigenomics, Roche Diagnostics and Applied Proteomics.

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## P0162 IS HYBRID ENDOSCOPIC SUBMUCOSAL DISSECTION EFFECTIVE FOR TREATMENT OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS? A SINGLE CENTER EXPERIENCE


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**Introduction:** There is wide variation in endoscopic treatment of large non-pedunculated colorectal polyps (LNPCP, Rutter et al., *Gut* 2015) among gastroenterology practices. Both endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) techniques are applied. The hybrid ESD (hESD) is an alternative resection technique, though its effectiveness in the treatment of LNPCPs is unclear. Because the learning-curve of ESD is steep and lengthy, hESD could be helpful as an intermediate step in acquiring technical skills. The aim of this study was to evaluate the complete resection rate and local recurrence rate of EMR and hESD in our daily practice.
**Aims & Methods:** We prospectively included all consecutive patients who underwent endoscopic resection of LNPCPs at a community hospital from January 2008 to October 2015. Follow-up data were collected. We defined LNPCPs as large (≥20 mm) sessile, flat, and depressed colorectal neoplasms or combinations (Paris classification). Overall complete resection rate was defined as complete resection after 1, 2 or ≥3 sessions. Early local recurrence was defined as presence of residual adenoma at first follow-up examination after resection. All procedures were performed by one experienced therapeutic colonoscopist.
**Results:** Thirty-five patients (mean age 74.9 yrs, 74.3% male) with 42 LNPCPs and 56 patients (mean age 69.8 yrs, 48.2% male) with 58 LNPCPs were included in the EMR group vs hESD group, respectively. Lesion characteristics and outcomes of resection are summarized in **Table 1**. Overall complete resection rate after 1, 2 or ≥3 sessions was 76.2%, 78.6% and 85.7% for EMR vs 74.1%, 87.9% and 89.7% for hESD. En-bloc resection rate was similar in the EMR group vs hESD group. Early recurrence rate after EMR and hESD was 23.8% (95% CI 12.1–39.5%) vs 25.9% (95% CI 15.3%-39%) after a median follow-up duration of 5.2 (1.2–24.4) months and 5 (0.7–14.9) months. Referral rate to surgery was similar in both groups. Two (4.8%) and 4 (6.6%) post procedural complications requiring hospital admission occurred after EMR vs hESD, without the need for surgery.

**Table 1:** Lesion characteristics and outcomes of EMR vs hESD. CRC: colorectal cancer, EMR: endoscopic mucosal resection, hESD: hybrid endoscopic submucosal dissection, HGD: high grade dysplasia, LGD: low grade dysplasia.

| Lesion characteristics | EMR (n = 42) | | hESD (n = 58) | |
|---|---|---|---|---|
| **Location** | | | | |
| Proximal | 21 | 50% | 12 | 20.7% |
| Distal | 21 | 50% | 46 | 79.3% |
| **Mean polyp size, mm** | 25.1 | [20-53] | 29.7 | [20-60] |
| **Polyp shape** | | | | |
| Sessile | 20 | 47.6% | 12 | 20.7% |
| Flat, depressed, combinations | 22 | 52.4% | 46 | 79.3% |
| **Histopathology** | | | | |
| Adenoma with LGD | 27 | 64.3% | 26 | 44.8% |
| Adenoma with HGD | 12 | 28.5% | 25 | 43.1% |
| Early CRC | 2 | 4.8% | 7 | 12.1% |
| Sessile serrated adenoma/polyp | 1 | 2.4% | 0 | 0% |
| **Overall complete resection rate** | | | | |
| After 1 session | 32 | 76.2% | 43 | 74.1% |
| After 2 sessions | 33 | 78.6% | 51 | 87.9% |
| After ≥3 sessions | 36 | 85.7% | 52 | 89.7% |
| **En-bloc resection rate** | 19 | 45.2% | 25 | 43.1% |
| **Early recurrence rate** | 10 | 23.8% | 15 | 25.9% |
| **Referral to surgery** | 2 | 4.8% | 3 | 5.2% |
| **Complication rate** | 2 | 4.8% | 4 | 6.8% |
| Bleeding | 1 | 2.4% | 2 | 3.4% |
| Abdominal pain | 1 | 2.4% | 2 | 3.4% |

(continued)

**Table 1**. Continued

| Lesion characteristics | EMR (n = 42) | | hESD (n = 58) | |
|---|---|---|---|---|
| Perforation | 0 | 0% | 0 | 0% |

**Conclusion:** To our knowledge, this is the first study to report outcomes of hESD of LNPCPs in the Netherlands. In this single-center experience, both EMR and hESD appeared to be safe and equally effective in resecting LNPCPs, albeit some cases require multiple sessions. Larger studies are needed to investigate whether hESD can help to speed-up the learning-curve of ESD.
**Disclosure of Interest:** S. Sanduleanu: Consultancy: Pentax Europe.
All other authors have declared no conflicts of interest.

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### P0163 APPROPRIATENESS AND YIELD OF SURVEILLANCE COLONOSCOPY IN FIRST-DEGREE RELATIVES OF COLORECTAL CANCER PATIENTS: A 5-YEAR FOLLOW-UP STUDY IN A POPULATION-BASED SCREENING PROGRAM

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**Introduction:** Appropriate surveillance colonoscopy according to guidelines is crucial for optimal effectiveness of colorectal cancer (CRC) prevention. Family history (FH) of CRC has been associated with an increased use of surveillance, but it is uncertain if first degree relatives (FDRs) are at increased risk of recurrent neoplasia.
**Aims & Methods:** To evaluate the adherence, appropriateness and colorectal findings of surveillance colonoscopy in a population-based screening program (Trentino, Italy) for FDRs of CRC patients. From December 2005 to November 2009, 1252 FDRs had screening colonoscopy. They received a letter in which timing of the next examination was reported, according to the current guidelines; individuals with complex FH (one CRC at age > 60 or two or more CRC) and normal colonscopy were assigned to follow-up within 5 years; individuals with simple FH (one CRC at age > 60 years) and normal colonscopy and those with normal colonscopy and no FH were assigned to follow-up within 10 years; individuals with non advanced adenomas (nAA: 1 or 2 adenomas, size < 10 mm; low grade dysplasia; tubular histology) were assigned to follow-up within 5 years and individuals with advanced adenomas (AA: size ≥ 10 mm; high grade dysplasia; (tubulo)villous histology) or with 3 or more adenomas were assigned to follow-up within 3 years, regardless of the complexity of FH. Exclusion criteria: age > 75 years at the time of the scheduled follow up, emigration from Trentino, significant comorbidities, diagnosis of hereditary CRC syndromes. The program is ongoing; for the study's purpose FDRs were followed from baseline colonoscopy until October 2015. We calculated uptake and appropriateness of colonoscopy; the timing was considerate appropriate if surveillance has been performed a 6-month period around guidelines interval; colonoscopy was classified early (overuse) if performed 6 months before the expected date of follow-up or late (underuse) if performed 6 months after the expected date; we also calculated the yield of finding neoplastic lesions and predictive factors for them. We compared these data with those of 765 individuals without FH who underwent screening colonoscopy in the same period (controls). For the purpose of this study, patients were divided in 6 risk groups according to FH and findings at index colonoscopy: group 1 (AA and positive FH), group 2 (nAA and positive FH), group 3 (no adenomas and positive FH), group 4 (AA and no FH), group 5 (nAA and no FH) and group 6 (no adenomas and no FH). The follow-up of this study is 5 years; for uptake analysis, we considered individuals scheduled within 5 years; for appropriateness and yield of colonoscopy, we considered also individuals who underwent colonoscopy even if surveillance was recommended within 10 years.
**Results:** 722 FDRs and 232 controls were scheduled for follow up within 5 years. Adherence to colonoscopy was significantly higher among FDRs than among controls (93% vs 48%; p < 0.001). On-time colonoscopy was significantly higher in FDRs vs controls (59.6 vs. 18.8%; p < 0.0001). Overuse was observed in 37.3% of group 2 and underuse in 30% of group 1. In multivariate analysis, younger age (≤50 vs >71 yrs, OR 8.87, 95% CI: 2.80 – 28.08; 51–60 vs. >71, OR 9.33, 95% CI: 3.00 – 28.99 and 61–70 vs. >71, OR 6.75, 95% CI: 2.18–20.92) female sex (vs. male, OR 1.43, 95% CI: 1.02 – 1.98), positive FH (simple FH vs no FH, OR 2.71 95% CI: 1.68 – 4.38 and complex FH vs. no FH, OR 15.23, 95% CI: 9.01 – 25.73) and neoplasia at screening colonoscopy (AA vs. no adenomas, OR 2.88, 95% CI: 1.73 – 4.81 and nonAA vs. no adenomas, OR 3.97, 95% CI: 2.62 – 6.02) are predictors of appropriate surveillance. No differences were found in cumulative risk of AA between FDRs and controls when compared according to risk group (group 1 vs group 4: 10.8 vs 16.1% p ns; group 2 vs group 5: 4.0 vs 1.4% p ns and group 3 vs group 6: 4.8 vs 5%). In multivariate analysis AA at follow up was associated with age (HR 1.04; 95% CI 1.00–1.09) and AA at screening colonoscopy (HR 4.52; 95% CI 2.01 – 10.14).
**Conclusion:** In an organized screening program, colonoscopy uptake is high among FDRs, but in 40% of them, timing of surveillance is still inappropriate. FH of CRC does not impact on the yield of AA at surveillance colonoscopy in a 5 year follow-up.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0164 PREVALENCE AND SEX SPECIFIC DIFFERENCES IN LOCALIZATION OF SERRATED POLYPS WITHIN A LARGE AUSTRIAN COLORECTAL CANCER SCREENING COHORT

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**Introduction:** Serrated lesions, including sessile serrated polyps/adenomas (SSA) and traditional serrated adenomas (TSA) are known to follow a different histopathological pathway and show different tumor characteristics than conventional adenomas following the adenoma-carcinoma sequence. A study by Brenner et al. showed female sex and proximal localization to be associated with higher prevalence of interval cancer. We therefore analyzed prevalence rates of serrated lesions in a large colorectal cancer screening cohort with regard to gender and localization.
**Aims & Methods:** 127,421 screening colonoscopies performed by 283 endoscopists between May 2012 and April 2016 were assessed. For evaluation of localization, we limited our analyzes to colonoscopies where one lesion was detected (n = 95,211).
**Results:** Patients mean age was 60.15 (SD = 9.62). Overall polyp detection rate was 38.62% (n = 49,206) and serrated lesion detection rate 1.78% (n = 2,277). In 24.22% (n = 23,056) of patients with one lesion, polyps were detected; 27.28% (n = 12,251) of men and 21.16% (n = 10,805) of women. 3.12% (n = 719) of those polyps were serrated lesions [2.60% (n = 318) in male and 3.71% (n = 401) in female screened individuals]. Both, SSA [2.12% (n = 260) of male; 3.03% (n = 334) of female patients] and TSA [0.47% (n = 58) in male; 0.62% (n = 67) in female patients] were detected more often in women than in men. SSAs occur in both, men and women more often in the proximal [60.00% (n = 156) in male; 66.47% (n = 222) in female] than in the distal colon [40.00% (n = 104) in male and 33.53% (n = 112) in female patients]. Interestingly in women TSA were located more frequently in the proximal (62.68% n = 42) than in the distal colon (37.31% n = 25), while in male patients the distribution was the opposite [37.93% (n = 22) proximal and 62.06% (n = 36) distal].
**Conclusion:** In conclusion, serrated lesions occur in 1.78% of patients undergoing screening colonoscopy with higher prevalence in women than in men. Interestingly in women, TSA, as well as SSA were more frequently located in the proximal than in the distal colon compared to male patients, were TSAs were more often located in the distal and SSAs in the proximal colon, which could explain the higher occurrence of interval cancer in female patients and in the proximal colon.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0165 PILOT RESULTS OF THE ECQI SELF-ASSESSMENT QUESTIONNAIRE TO EVALUATE QUALITY IN COLONOSCOPY IN EUROPE

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**Introduction:** Awareness of quality indicators and the use of international best practice standards can improve the quality of colonoscopy.[1] The European Colonoscopy Quality Investigation (ECQI) Group is a team of experienced colonoscopists, from eight European Union countries. It seeks to improve clinical practice standards by helping colonoscopists perform a self-assessment.
**Aims & Methods:** To assess the quality of colonoscopy in current clinical practice versus quality standards[2, 3] established by the European Society of Gastrointestinal Endoscopy, through the use of a novel online questionnaire.

The questionnaire was tested via 2 pilots. Issues identified in the first pilot were refined for the second which concluded in July 2015.

**Results:** A range of data for individuals, institutions and countries was analysed. Seventy-seven practitioners at 22 institutions in 9 European countries completed questionnaires for 1, 548 colonoscopies. Nine institutions (41%) reported recording adenoma detection rate. Fourteen institutions (64%) used a bowel cleansing scale. Among these, 10 (46%) used the Boston Bowel Preparation Scale and 4 (18%) used their own scale. Caecal intubation rate was used routinely by 52 (68%) practitioners. Other measured quality indicators were used only by a minority of the practitioners (Table 1). The main reasons for colonoscopy were clinical signs and symptoms 694 (45%) including altered bowel habit 264 (17%), rectal bleeding 227 (15%), pain 185 (12%), and other causes 151 (10%). Screening was also a common reason [following a positive screening test in 17%, due to familial risk 6% and without a pre-screening test 5%]. The intended endpoint (IE) was reached in 1, 419 (92%) procedures, and was most frequently the caecum 69%, ileum 27%, or anastomosis 3%; 1% not answered (NA). Reasons for not reaching IE, 72 (5%) were: technically difficult 20 (1%), insufficient preparation 18 (1%), stricture 18 (1%), and pain 11 (1%). Bowel cleansing was rated as adequate on the BBPS in 1, 180 (76%) procedures, and inadequate in 318 (21%) cases; NA 50 (3%).

**Table 1:** Recording of quality measures by practitioners.

| Do you routinely record | Yes (%) | No (%) | Not answered (NA) (%) |
|---|---|---|---|
| Adenoma detection rate? | 29 (38%) | 47 (61%) | 1 (1%) |
| Caecal intubation rate? | 52 (68%) | 25 (32%) | 0 (0%) |
| Polyp detection rate? | 29 (38%) | 48 (62%) | 0 (0%) |
| Polyp removal rate? | 31 (40%) | 44 (57%) | 2 (3%) |
| Polyp retrieval rate? | 25 (32%) | 51 (66%) | 1 (1%) |
| Retraction time? | 36 (47%) | 41 (53%) | 0 (0%) |
| Tattoo rate? | 21 (27%) | 56 (73%) | 0 (0%) |

**Conclusion:** This 2nd pilot has proven the relevance of this questionnaire, enabling colonoscopists to gather information on quality in an easy to use, yet comprehensive manner. It will now be utilised in a wider activation phase across Europe, and may provide useful information on colonoscopy, enabling the identification and improvement of quality issues.

**Disclosure of Interest:** R. Jover Martínez: Advisory board participant for Norgine.
A. Agrawal: Advisory board participant for Norgine.
P. Amaro: Advisory board participant for Norgine.
L. Brink: Advisory board participant for Norgine.
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### P0166 THERAPEUTIC STRATEGY OF ESD FOR COLORECTAL TUMORS ACCOMPANIED BY SEVERE DEGREE FIBROSIS IN THE SUBMUCOSAL LAYER


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**Introduction:** The development of the ESD technique has led to changes in therapeutic strategies for early colorectal cancer. The difficulty of one-piece resection of a colorectal tumor using ESD depends on the existence of fibrosis rather than the tumor size. We examined the causes and endoscopic findings of fibrosis in the submucosal layer (SM) in order to establish an appropriate therapeutic strategy for such lesions.

**Aims & Methods:** We performed ESD on 1, 229 colorectal tumors in 1, 197 patients (male: female = 700:497; mean age, 65.9years). Among these 1, 229 cases, 278 cases were accompanied by fibrosis in the SM. These cases were divided into three groups; absence of fibrosis (type A), fibrosis due to benign causes (due to biopsy, recurrence after EMR, etc. type B), and fibrosis due to cancer invasion in the SM layer (type C). The degree of fibrosis was classified into mild (grade 1), moderate (grade 2), and severe (grade 3) degree. In this study, we analyzed these lesions in order to establish a safe and curative ESD technique.

**Results:** These 278 cases accompanied by fibrosis were including 12 withdrawal cases, 96 cases were considered related to cancer invasion (type C), and 182 cases were related to benign cause (type B). The one-piece resection rates were as follows: Type A; 925/751 (97.3%), type B-1; 84/87 (96.6%), B-2:46/52 (88.5%), B-3:25/43 (58.1%), type C-1:46/46 (100%, average SM depth:692.2$\mu$m), C-2:19/20 (95.0%, average SM depth:1, 772.7$\mu$m), C-3:18/31 (58.1%, average SM depth:2, 716.8$\mu$m). We had experienced four cases (Type A:1, Type B:3) with perforation (0.3%) and 14 cases with postoperative bleeding (1.1%). Among these cases complicated with perforation, two cases were treated with clipping conservatively and other two cases required emergent surgery due to peritonitis. The tumors accompanied by mild to moderate fibrosis should be dissected carefully just above the muscle layer. In cases accompanied by severe degree fibrosis (type B-3), ESD becomes more difficult due to the risk of perforation. From the analysis of one-piece resection cases in type B-3, we developed the safe ESD technique to break these difficulties. The feasibilities to complete one-piece resection with type B-3 were as follows: 1) recognition of the narrow translucent area just above the muscle layer, 2) identification of the dissection line by linking with the normal SM layer of both ends of fibrosis, 3) using an endo-clip on the muscle layer to prevent perforation before dissection. Other cases of type B-3 were impossible to design the dissection line due to wide and firm fibrosis. The limitation of ESD is thought to be existed in these lesions from the viewpoint of safety and curability. From these reasons, we established the laparoscopy endoscopy cooperative surgery (LECS) procedure to complete a safe one-piece resection with adequate surgical margin. Otherwise, type C-3 was showing a deep cancer invasion about 3, 000$\mu$m in the SM, and revealed very low one-piece resection rate. From these results, type C-3 endoscopic finding was thought to be an indication of laparoscopic surgery (LAC) due to the risk of lymph node metastasis.

**Conclusion:** The usefulness of ESD for lesions with fibrosis is limited from the viewpoint of safety and curability. We classified the endoscopic findings of fibrosis in order to establish a safe and curative ESD technique. The tumors accompanied by fibrosis of a mild to moderate degree become a standard indication for ESD. And the tumors accompanied by severe degree fibrosis without deep cancer invasion in the SM will become a relative indication of ESD and laparoscopy endoscopy cooperative surgery (LECS) procedure.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0167 "OVER-THE-SCOPE" CLIP (OTSC) DECREASES THE SURGERY RATE IN THE MANAGEMENT OF IATROGENIC PERFORATIONS OCCURRING DURING ENDOSCOPIC PROCEDURES


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**Introduction:** Perforation is one of the most serious complications of diagnostic and therapeutic endoscopic procedures. The over-the-scope clip (OTSC; Ovesco Endoscopy AG, Tubingen, Germany) is a relatively new endoscopic tool used for closure of luminal perforations. In contrast to through-the-scope clips, the OTSC is able to capture a larger volume of tissue with a higher compression force.

**Aims & Methods:** The aim of this study is to compare the management of iatrogenic perforations before and after the OTSC was available in our endoscopy unit. We conducted a monocentric retrospective study from June 2007 to June 2015. All iatrogenic gastrointestinal perforations occurring during an endoscopic procedure and detected during the procedure were included in the study, irrespective of the location of the perforation. The study was divided in two equal periods of time: a period before the use of the OTSC, from June 2007 to June 2011, and a period during which the OTSC was available, from June 2011 to June 2015. In both periods, all patients had a multidisciplinary management involving the gastroenterologists, the surgeons and the intensive care physicians. The primary endpoint was to compare the rate of surgery between the two groups. The secondary endpoint was to compare the mortality rates between the two groups.

**Results:** During the first period of the study (from June 2007 to June 2011), 24 perforations were recorded for 29203 endoscopies performed (18 in the colon, 5 in the duodenum and one in the stomach). 15 of the 24 perforations (62.5%) were referred for surgery, and the mortality rate during this period was 8.3% (2/24). During the second period (from June 2011 to June 2015), 16 perforations were reported for 35525 endoscopies performed (9 in the colon, 4 in the duodenum, 2 in the stomach and one in the esophagus). In eleven patients, an OTSC was used to close the perforation, with a technical success achieved in 100% since all patients had an adequate deployment of the OTSC and a complete sealing of the perforation without leakage. However two of these patients had to undergo surgery despite an adequate closure of the perforation: one because of a localized peritonitis and the other because the clip deployed in the sigmoid had captured the right ureter. The rate of surgery during this period was 12.5% (2/16) versus 62.5% ($p = 0.002$), and the mortality rate was 0% versus 8.3% but the difference was not significant ($p = 0.23$).

**Conclusion:** The OTSC system is effective for endoluminal closure of acute iatrogenic perforations and results in a significant decrease in the surgery rate. Based on our experience, all endoscopy units should have a supply of OTSC, with a proper training for endoscopists and nurses on its use.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0168 CURRENT STATUS OF ERAT IN THE MANAGEMENT OFACUTE APPENDICITIS IN CHINA

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**Introduction:** Endoscopic retrograde appendicitis therapy (ERAT) is a new method for the treatment of acute appendicitis. The study aims to analysis the information of ERAT and to prove the safety and efficacy of this method.
**Aims & Methods:** The study was performed on patients underwent ERAT at 8 tertiary hospitals in China from 2009 to 2014. The inclusive criteria: patients clinically suspected of acute appendicitis (Alvarado scores $\geq 5$); the diagnosis can be made by ultrasonography or CT scan. The main outcome was clinical success rate. The secondary outcomes included the success rate of cannulation, time of resumption of diet, hospital stay, hospital costs, complications and recurrent rate.
**Results:** One hundred eighteen of 158 patients underwent ERAT were enrolled into the study. There were 107 of 118 patients (91%) who had successfully cannulating appendiceal orifice. One hundred of them (including 6 patients with peri-appendiceal abscess) had definite diagnosis of acute appendicitis and received ERAT. The median time of abdominal pain and abdominal tenderness relief was 12 hours (Inter quartile range, IQR = 6 hours-72 hours) and 24 hours (IQR = 24 hours -72 hours) respectively. The clinical success rate was 97%. The median time of hospital stay was 3 days (IQR = 2 days–4 days). The median of hospital costs was 8497 RMB (IQR = 5303 RMB-12358 RMB). The rate of complications was 2%. During the median time of following up (12 months, IQR = 5–24 hours), the recurrent rate was 7%.
**Conclusion:** This study confirmed the safety and utility of ERAT for the diagnosis and treatment of acute appendicitis and peri-appendiceal abscess. However, further studies need to further improve the novel method.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0169 SURVEILLANCE AFTER COLORECTAL CANCER RESECTION: THE ROLE OF COLONOSCOPY

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**Introduction:** The postoperative surveillance of patients treated for colorectal cancer (CRC) is intended to prolong survival by diagnosing recurrent and metachronous cancers at a curable stage, and to prevent metachronous cancer by detection and removal of precancerous polyps.
**Aims & Methods:** To evaluate the rates of local relapses, synchronous and metachronous cancers and adenoma detection (AD) in surveillance colonoscopies and to identify clinical characteristics associated with AD in a cohort of patients with CRC treated with curative intent. Cohort study, single-centre. All patients with CRC, stages II and III AJCC, treated with curative intent, with at least one surveillance colonoscopy between 03/2008 and 07/2015, were included. Surveillance colonoscopies were done in the 1st (or within 3–6 months postoperatively when the baseline colonoscopy was incomplete) and 4th years after CRC resection; Tumours detected during the 1st year after CRC diagnosis were considered synchronous. Statistical analysis was performed with SPSS v20.0, using chi-square test and a multivariate regression model.
**Results:** 391 patients were evaluated; mean age was $65 \pm 10$ years; 59.8% male; tumour location: rectum-51.2%, left colon-29.9%, right colon-18.9%; Baseline colonoscopy: 34.5% had an incomplete colonoscopy, synchronous cancers in 4.3% and adenomas in 31.5%. During follow-up: 36.6% had adenomas and 2.6%: local relapse (n = 5), synchronous (n = 3) or metachronous (n = 2) cancer; 182 patients underwent two surveillance examinations. 1st year AD: 31.7%, 4th year AD: 29.7%. AD in the 1st surveillance colonoscopy was positively associated with AD on the 4th year ($p = 0.001$). After multivariate analysis, the factors associated with AD were male gender ($p = 0.01$) and left colon tumours ($p = 0.011$).
**Conclusion:** The higher adenomas' detection rate in patients with left colon tumours is likely related to the high rate of incomplete baseline colonoscopies due to malignant obstruction or inadequate cleaning. During postoperative surveillance more than one third of patients had adenomas and 2.6% local relapse or synchronous/metachronous cancers, which highlights the importance of endoscopic surveillance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0170 BEYOND WHITE LIGHT: EMBARKING ON THE FIRST EXPERIENCE WITH THE NEW GREEN-RED-ORANGE LIGHT OPTICAL ENHANCEMENT MAGNIFICATION COLONOSCOPY TO DEFINE SUBTLE INFLAMMATORY CHANGES IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** The i-SCAN Optical Enhancement (OE) with CloseFocus™ (Pentax, Japan) is a recently introduced novel virtual chromoendoscopy (CE) platform which enhances the details of the surface structures of blood vessels and the glandular –crypts structures of the colonic mucosa in much higher resolution than white light. Thus, the OE-iSCAN technology with CloseFocus ™along with novel digital-based CE features (i.e., surface, contrast, tone and OE) have the potential to improve characterization of mucosal and vascular patterns and to increase the accuracy of assessing and predicting grade of inflammation and mucosal healing in ulcerative colitis (UC) patients.
**Aims & Methods:** We aimed to determine whether OE-iSCAN CloseFocus™ (Pentax, Japan) has the potential to assess more accurately the disease activity in patients with UC as compared with white light Mayo endoscopic score, relative to the recently validated Robarts Histology Index (RHI) and the newly defined histological ECAP score.[1] Consecutive patients with UC undergoing the new OE-iSCAN –EPKi 7010 with Close Focus™ (Pentax, Japan) were enrolled for assessment of the grade of inflammation and mucosal healing. Inflammation and mucosal healing in UC were recorded according to Mayo endoscopic subscore (0–3) and CE score was divided into mucosal and vascular pattern as well as overall score. Subsequently targeted endoscopic biopsies were obtained for histological analysis of disease activity (RHI) and the ECAP score. [1]

The diagnostic accuracy of OE-CE was calculated with histology as a gold standard.
**Results:** 50 consecutive patients (41 UC and 9 control) were included in the study (25 men, median age 49 y, range 24–79). The endoscopic appearance by overall OE-iSCAN score correlated with ECAP ($r = 0.70$; $p < 0.0001$) and the accuracy of OE-iSCAN to detect abnormalities by ECAP was 80% (sensitivity 77.7%; specificity 100%). The correlation between Mayo endoscopic score and ECAP score was less strong ($r = 0.432$; $p < 0.001$). Both the OE-iSCAN vascular and mucosal scores correlated with ECAP score ($r = 0.65$ and 0.71 respectively; $p < 0.001$). We also determined correlation between OE-iSCAN score and RHI ($r = 0.61$; $p < 0.01$) and the accuracy to detect abnormalities by RHI was 68% (sensitivity 78.1% specificity 50%). The RHI unlike ECAP only scores acute but not chronic histological changes.
**Conclusion:** The new OE-iSCAN with magnification may accurately reflect histologic abnormalities demonstrated by ECAP histology score which incorporates the full spectrum of acute and chronic histologic abnormalities. This demonstrates that with advanced CE technology, endoscopic assessment of UC is starting to approximate histology.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0171 REMOVAL OF DIMINUTIVE COLORECTAL POLYPS: A PROSPECTIVE RANDOMIZED COMPARATIVE STUDY BETWEEN COLD SNARE POLYPECTOMY AND HOT FORCEPS BIOPSY

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**Introduction:** Cold snare polypectomy (CSP) is a common method for resecting diminutive polyps without using submucosal injections or electrocautery. Hot forceps biopsy (HFB) is another method for removing diminutive polyps and is still widely used because it is comparatively easy to manipulate. However, there have been no definitive studies to compare these two techniques directly.
**Aims & Methods:** The aim of this study was to compare the efficacy and safety of CSP and HFB for the removal of colorectal diminutive polyps. The study design was a prospective, randomized, single-center comparison of two methods between CSP and HFB in patients with diminutive colorectal polyps 3–5 mm in size from December 2014 to October 2015. The consecutive patients >20 years old with polyps of target size were enrolled. Exclusion criteria were patients with inflammatory bowel disease, patients with polyposis, polyps suspicious of cancer, and hyperplastic polyps less than 5 mm in the distal colon.
**Results:** After a written informed consent was obtained, 208 patients with a total of 339 polyps were randomized into CSP group (102 people) and HBF group (106 people). After the exclusion of some polyps, 283 polyps (CSP group:148 polyps, HFB group:135 polyps) were evaluated. There was no significant difference between the groups with respect to demographic characteristics of the patients and polyps. The en-bloc resection rate was significantly higher with CSP than HFB (99.3% [147/148] vs 80.0% [108/135], $p < .0001$). The complete resection rate was significantly higher with CSP than HFB (80.4% [119/148] vs 47.4% [64/135], $p < .0001$). Immediate bleeding rate was similar (8.6% [13/148] vs 8.1% [11/135], $p = 1.000$) and hemostasis with clips was successful in all the cases. No perforation or delayed bleeding was encountered. The rate of severe tissue injury to the pathological specimen was higher in the HFB than in the CSP (52.6% [71/135] vs 1.3% [2/148], $p < .0001$). The frequency of polyp retrieval failure was higher in the CSP than in the HFB (9/183 polyps vs 0/156).
**Conclusion:** The results showed that CSP is more effective than HFB for resection of diminutive polyps. Endoscopic en-bloc resection rate and pathologic complete resection rate were both lower in HFB group as histological evaluation in HFB was difficult due to tissue injury. Serious events were not encountered in either group. A further study including long-term follow-up is required. (Clinical trial registration number: UMIN000015016).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0172 A 5.9MM ENDOSCOPE CAN RELIEVE ABDOMINAL PAIN EFFECTIVELY IN UNSEDATED WATER-AIDED COLONOSCOPY

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**Introduction:** Although standard colonoscopy by water exchange or using an endoscope with a diameter of 9.2 mm can relatively reduce patients' abdominal pain, there are still around 5% of them who can not endure it and another 5% described the pain as moderate during the procedure.
**Aims & Methods:** Aims: To detect that if abdominal pain can be relieved effectively by using a 5.9 mm endoscope with water exchange in unsedated colonoscopy. Methods: The patients who described the abdominal pain as moderate or serious (the visual analog score > 5) during standard colonoscopy without sedatives by using water exchange were enrolled. All of them were to undergo an unsedated water-aided colonoscopy by using a 5.9 mm endoscope. The abdominal pain score (on a 10-cm unscaled visual analog; 0 = no pain, 10 = serious pain) after the cecal intubation was documented as the primary outcome.
**Results:** A total of 57 patients were enrolled. During the last standard colonoscopy, the proportions of the abdominal pain scores of 5, 6, 7, 8, 9 and 10 were 12% (7/57), 12% (7/57), 23% (13/57), 11% (6/57), 5% (3/57) and 37 (21/57), repectively. The medium pain score was 8. While in this study, the highest pain score was only 3. The proportions of the abdominal pain scores of 0, 1, 2 and 3 were 68% (39/57), 12% (7/57), 12% (7/57) and 7% (4/57), respectively. The medium pain score was 0. It was much lower when compared to before ($P < 0.001$).
**Conclusion:** In this study, only a minority of the patients described the abdominal pain as mild. Whereas the others hardly felt uncomfortable during the procedure by using a 5.9 mm endoscope.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0173 A COMPARATIVE STUDY OF PROPOFOL VERSUS PROPOFOL–FENTANYL FOR SEDATED COLONOSCOPIES BY NON-ANESTHESIOLOGIST

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**Introduction:** Gastrointestinal endoscopies are invasive, unpleasant and sometimes painful procedures. Sedation is essential to reduce the anxiety, pain and also to increase their efficacy. Various sedation and analgesia regimens can be used, such as midazolam, fentanyl and propofol. Propofol is considered the best single sedation agent for endoscopy. Our purpose was to compare propofol alone and in combination with fentanyl for sedated colonoscopies.
**Aims & Methods:** We prospectively recorded all the colonoscopies performed in our center between July 2013 and July 2015. During the first year we administered propofol at an initial dose of 0.5–1 mg/kg and a fixed dose of 50 mcg of fentanyl. The second year we only used propofol in monotherapy. Demographic data, anesthetic risk, propofol dose, adverse events, and patient and physician satisfaction (scale: 1 very good; to 4, bad) were obtained. We excluded incomplete procedures, not sedated by the endoscopist, and patients with two endoscopic procedures performed on the same day. Statistical analysis was performed with the SPSS v20.0 software.
**Results:** During the study period 4741 colonoscopies were performed. 2223 were sedated with propofol-fentanyl and 2518 with propofol. Table 1 shows the demographics, propofol dose, complications and satisfaction in both groups. There were significant differences between groups in the mean propofol dose (propofol-fentanyl group: $132.4 \pm 59.5$ mg, propofol monotherapy group: $160.2 \pm 69.1$ mg, $p < 0.05$) and in therapeutic procedures (propofol-fentanyl: 24%, propofol monotherapy: 38.8%, $p < 0.05$). When therapeutic colonoscopies were excluded, the difference in the propofol dose persisted ($154.7 \pm 59$ mg vs $129 \pm 53$ mg, $p < 0.05$). There were no differences in adverse events. No serious adverse event occurred. The satisfaction for patients and endoscopists were very good in the majority of cases.

**Table 1:** Demographic, propofol dose, adverse events, complications and satisfaction in both groups.

| CHARACTERISTICS | PROPOFOL (n = 2518) | PROPOFOL-FENTANYL (n = 2223) |
|---|---|---|
| Age | $55.2 \pm 15.1$ | $55.7 \pm 15.4$ |
| Weight | $73.9 \pm 15.3$ | $73.8 \pm 14.7$ |
| ASA I/II/III (%) | 45.7/52.3/2 | 57.3/40.9/1.8 |
| Propofol Dose | $160.2 \pm 69.1$* | $132.4 \pm 59.5$ |
| Therapeutic (polypectomy)% | 38.8* | 24 |
| Adverse events (%) Desaturation/Bradycardia/Hypotension | 0.4/0.5/0.1 | 0.6/0.6/0.1 |
| Satisfaction (very good-good) Patient/Endoscopist | 99.5/98.3 | 99.8/99.8 |

Data are presented as mean ± SD (range: 95% CI of the mean). Abbreviations:ASA (American Society of Anesthesiology). *P < .005.

**Conclusion:** In our experience, the use of propofol in monotherapy was as effective as the use of propofol plus fentanyl, without decreasing the pleasant perception for the patient and the endoscopist. Additionally, the use of a single drug simplifies the daily practice, reducing the possibility of mistakes with medications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0174 DIAGNOSTIC ABILITY OF AUTOMATED DIAGNOSIS SYSTEM USING ENDOCYTOSCOPY FOR INVASIVE COLORECTAL CANCER

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**Introduction:** Endocytoscopy (EC) enables in vivo observation of nuclei at 380-fold magnification during gastrointestinal endoscopy (1). We have developed a computer-aided diagnosis system for EC imaging (EC-CAD) that provides fully automated classification of colorectal polyps and reported its usefulness (2, 3). The aim of the present study was to evaluate the efficacy of EC-CAD system for diagnosis of invasive colorectal cancer.
**Aims & Methods:** EC-CAD comprises image acquisition, nuclear segmentation, feature extraction, and classification into three pathological groups (non-neoplastic, adenoma and invasive cancer). The classification algorithm was programmed based on 350 features of each image (e.g., area, circularity, diameter, and perimeter of nuclei, and over 300 variables calculated by texture analysis of a whole image). We used a support vector machine to help classify these many features; 5543EC images (2506 non-neoplastics, 2667 adenomatous and 370 invasive cancerous lesions) were used for machine learning in the process of construction of the model. A total of 300 EC images (100 non-neoplastic, 100 adenomatous and 100 invasive cancerous lesions that had not been used for machine learning) are used for test data.
**Results:** Of all the 300 test images, 284 images were assessable with EC-CAD system (94.7%). EC-CAD system provided sensitivity of 84.0%, specificity of 99.5%, positive predictive value of 98.8%, negative predictive value of 92.6%.
**Conclusion:** This study indicates the usefulness of EC-CAD system for diagnosing invasive colorectal cancer. The EC-CAD system has the possibility to develop its diagnosis ability as study sample of invasive cancerous lesions increase.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0175 EXTRA WIDE ANGLE VIEW COLONOSCOPE (EWAVE) HAS SUPERIOR POLYP DETECTION RATE WHEN COMPARED TO A STANDARD COLONOSCOPE (SD): A RANDOMISED TANDEM PRE-CLINICAL STUDY

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**Introduction:** Colonoscopy screening with the removal of adenomas has been the preferred and most effective strategy to prevent colorectal cancer (CRC). However adenomas are often missed during colonoscopic examination, particularly on the proximal sides of folds and at the flexures. The prototype (EWAVE) Extra Wide Angle View colonoscope (Olympus, Tokyo, Japan) has a 147°- 235° angle lateral/backward view lens and a standard 140° angle forward view lens. Views from both lenses are constructed and displayed as a single image. By improving visualisation behind the folds and flexures this new scope could increase the polyp detection rate (PDR).
**Aims & Methods:** Aims To compare the polyp detection rate between EWAVE and a standard colonoscope in a colonic model with simulated polyps. **Methods** Two colorectal (Koken, Japan) rubber colon models were prepared with 18 and 20 polyps of different size (5–20 mm) at various locations. Seventeen endoscopists, 14 gastroenterology trainees and 3 nurse endoscopists with varying levels of experience performed back to back examinations with the standard colonoscope and EWAVE scope. The order which they performed the procedure (i.e. EWAVE or SD first) was randomised using concealed envelopes. In order to minimise type 2 error, on the 2nd model the endoscopists performed the procedure in reverse order.
**Results:** There was no significant difference in mean insertion time ($p = 0.8$) or withdrawal time ($p = 0.29$) between EWAVE and standard colonoscope (Figure 1). Mean simulated PDR was significantly higher with EWAVE examination when compared to standard colonoscopic examination in both models ($p = 0.026$ and $< 0.0001$). Mean simulated PDR was significantly higher with EWAVE in comparison to the standard colonoscope for polyps in the mid transverse colon (79.4% vs 32.3%, $p = 0.0002$) and mid sigmoid colon (82.3% vs 52.9%, $p = 0.0186$). When the examination was carried out with the standard colonoscope followed by EWAVE, PDR was significantly higher in both models ($p = 0.045$ for model 1 and $p < 0.0001$ for model 2). More significantly no difference was observed when the procedure was performed in the reverse order ($p = 0.28$ for model 1 and $p = 0.08$ for model 2).

| | Model I Standard | Model I EWAVE | P value | Model II Standard | Model II EWAVE | P value |
|---|---|---|---|---|---|---|
| Insertion time (mean+/- SD) | 3.7+/-1.8 | 3.74+/-1.4 | 0.89 | 3.05+/-1.7 | 2.89+/-1.7 | 0.80 |
| Withdrawal time (mean+/- SD) | 4.88+/-1.8 | 4.96+/-2.1 | 0.91 | 4.81+/-3.0 | 3.85+/-1.6 | 0.29 |
| PDR (mean+/-SD) | 14.5+/-1.8 | 15.93+/-1.3 | 0.026 | 15.8+/-1.2 | 18.13+/-1.5 | <0.0001 |

**Conclusion:** Our non-clinical study showed significantly higher polyp detection rates with the novel extra wide angle colonoscope when colonoscopy was performed by moderately experienced colonoscopists. Further clinical trials appear warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0176 THE FREQUENCY OF THE INAPPROPRIATE CONVERSION FROM COLONOSCOPY TO SIGMOIDOSCOPY AND ITS POTENTIAL EFFECT ON QUALITY INDICATORS

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**Introduction:** A caecal intubation rate of >90% is a well-accepted quality indicator of colonoscopy and is consequently monitored within endoscopy units. Endoscopists' desire to meet this target may mean that incomplete colonoscopies are recorded as flexible-sigmoidoscopies.
**Aims & Methods:** The aim of this study was to examine whether the conversion of requested colonoscopies is a clinically significant phenomenon. A retrospective review of all flexible-sigmoidoscopies performed between 1st January 2015 and 31st December 2015 was performed across three UK teaching hospitals; Nottingham University Hospitals, Sheffield Teaching Hospitals and Cambridge University Hospitals. Where a colonoscopy was requested but a flexible sigmoidoscopy performed, the patient's records and endoscopy reports were reviewed to determine whether this conversion was appropriate.
**Results:** During the 12-month period, 6839 flexible-sigmoidoscopies were performed. 149 requests could not be retrieved and were therefore excluded from this analysis. Of the 6690 sigmoidoscopy requests reviewed, 2.8% (n = 190) procedures were originally requested as a colonoscopy, with 32 converted prior to commencing the procedure on clinical grounds. 53 of converted procedures were planned polypectomies or post polypectomy assessments in patients who had previously undergone complete visualisation of the colon, and could therefore be considered appropriate to the intended purpose. 105 conversions occurred in patients who had a valid documented indication for colonoscopy and had undergone full bowel preparation. The most common reasons cited included poor bowel preparation (n = 38), technically challenging (n = 30) or clinically inappropriate (n = 26). A clear reason for conversion was not apparent in 11 cases. During the study period 21943 colonoscopies were performed and so inappropriate conversions represent 0.48% of the total requests. This practice was observed amongst 44 endoscopists, when inappropriate conversions were included in individuals' performance data 6 endoscopists fell to ≤90% target caecal intubation target, whilst a further 9 who were already below this target demonstrated poorer performance.
**Conclusion:** A small, but significant number of colonoscopies are converted to flexible sigmoidoscopies at the time of the procedure. This study demonstrates the conversion of colonoscopy to sigmoidoscopy as being a potential limitation of relying on caecal intubation rate alone. Endoscopy units should consider monitoring the rate of inappropriate conversions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0177 CORRELATION BETWEEN ADENOMA DETECTION RATE AND SERRATED ADENOMA DETECTION RATE IN AN UNSELECTED POPULATION

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**Introduction:** Serrated lesions of the colon and rectum are precursors of colon cancer. However, they are often difficult to detect and missed serrated lesions in the proximal colon are implicated in post colonoscopy interval cancers. Adenoma detection rate (ADR) has been established as a key quality marker in colonoscopy. Improvements in adenoma detection rates are asociated with a reduction in colorectal cancer risk. The correlation between adenoma detection rate (ADR) and serrated adenoma detection rate (SSADR) is not well established. It is postulated that serrated adenoma detection rate may be a more stringent marker of quality.

**Aims & Methods:** The aim of our study was to assess the correlation between adenoma detection rate and serrated adenoma detection rate in an unselected population. Procedures performed in our endoscopy unit over an 18 month period between July 2014 and December 2015 were considered for the retrospective analysis. ADR and SSADR were calculated for each proceduralist for all procedures they performed during the study period. ADR and SSADR were also calculated separately for all procedures for patients $>50$ years. Detection rates were expressed as number of procedures with at least one adenoma or serrated adenoma detected. Statistical anlysis was performed with Spearman's correlation co-effiecient to assess the strength of association between ADR and SSADR.

**Results:** 13 endoscopists performed 3173 procedures during the study period. 8 of them were physicians and 5 were surgeons. Individual results were as follows.

| Endoscopist | ADR | SSADR | >50yrs ADR | >50 yrs SSADR |
|---|---|---|---|---|
| 1 | 36.2% | 9.8% | 44.2% | 9.6% |
| 2 | 47.8% | 18.3% | 61.4% | 18.2% |
| 3 | 31.3% | 7.4% | 38.9% | 9.2% |
| 4 | 39.8% | 8.2% | 44.4% | 7.8% |
| 5 | 30.2% | 8.9% | 37.4% | 9.2% |
| 6 | 37.9% | 8.9% | 44.3% | 6.8% |
| 7 | 27.7% | 6.1% | 36.4% | 7.6% |
| 8 | 23.7% | 6.1% | 26.3% | 7.5% |
| 9 | 33.3% | 12.3% | 50.0% | 21.0% |
| 10 | 33.5% | 12.7% | 45.2% | 14.5% |
| 11 | 44.0% | 6.3% | 47.0% | 6.0% |
| 12 | 38.1% | 12.2% | 47.8% | 15.7% |
| 13 | 46.6% | 18.8% | 55.3% | 19.7% |

Statistical analysis suggested a positive association between ADR and SSADR ($r=0.56$, p0.04). When the analysis was performed for ADR and SSADR in the patient population $>50$ years, a stronger positive association between the 2 variables was detected ($r=0.64$, p 0.016).

**Conclusion:** Our study suggests a positive correlation between adenoma detection rate and serrated adenoma detection rate in an unselected population. A focus on improvement in quality in colonoscopy with a resultant increase in adenoma and serrated adenoma detection rate is vital in colorectal cancer prevention.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0178 RISK FACTORS FOR DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR COLORECTAL TUMORS IN JAPANESE PATIENTS

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**Introduction:** Endoscopic submucosal dissection (ESD) has been widely accepted as curative treatment for early gastrointestinal neoplasms. However, when performing ESD for colorectal neoplasms, the intestinal wall is relatively thin, and the lumen is narrow; therefore, the endoscopic manipulation of removing colorectal neoplasms is difficult. The main complications of colorectal ESD are intestinal perforation and delayed bleeding as well as gastric ESD. Therefore, the assessment and prediction of risk factors for complications in colorectal ESD are considered to be necessary. The risk factors for perforation during colorectal ESD have recently been investigated in several studies. However, there were few studies that assessed the risk factors for delayed bleeding after ESD for colorectal tumors. In this study, we aimed to clarify the risk factors for delayed bleeding after colorectal ESD.

**Aims & Methods:** This study included 124 consecutive colorectal neoplasms resected using ESD between April 2013 and November 2015. We classified patients and lesions into two groups on the basis of presence or absence of delayed bleeding and retrospectively compared the clinicopathological characteristics and clinical outcomes of ESD between the two groups.

**Results:** Delayed bleeding occurred in 10 (8.1%) of 124 lesions. Only one case of delayed bleeding required endoscopic hemostasis. With respect to patient-related factors, there was no significant difference between the two groups in mean age, sex, comorbidities, and current use of antithrombotic agents. With respect to lesion-related factors, there was no significant difference between the two groups in mean lesion size, growth pattern, resected tumor size, and mean procedure time. However, lesions located in the rectum (vs colon, $p<0.05$) were significantly related to delayed bleeding. The median number of occurrences of arterial bleeding during ESD was significantly higher in the delayed bleeding group (5, range: 0–20) than in the non-delayed bleeding group (1, range: 0–22) ($p<0.05$). Upon multivariate analysis, 3 and more occurrences of arterial bleeding during ESD (less than 2, odds ratio: 5.95; 95% confidence interval: 1.41–25.14; $p=0.02$) were significantly related to delayed bleeding after colorectal ESD, and lesions located in the rectum (vs colon, odds ratio: 4.54; 95% confidence interval: 0.89–23.16; $p=0.06$) were considered to relate to delayed bleeding after colorectal ESD.

**Conclusion:** This study demonstrated that frequent occurrences of arterial bleeding during ESD and location of tumors in the rectum were significant independent risk factors for delayed bleeding after ESD for colorectal neoplasms. Optimal management for patients with rectal tumors treated by ESD should be considered to avoid delayed bleeding after ESD regardless of patients' characteristics, tumor sizes, or tumor growth patterns.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0179 EFFICACY AND SAFETY OF THE NOVEL 1 L PEG AND ASCORBATE BOWEL PREPARATION NER1006 VERSUS STANDARD 2 L PEG WITH ASCORBATE IN OVERNIGHT OR MORNING SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY MORA

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**Introduction:** Successful colon cleansing enables effective colonoscopy. PEG-based split dosing preparations are the gold standard in cleansing, but many still require a high preparation volume intake. NER1006 is the first 1 L PEG3350 and ascorbate bowel preparation in phase 3 clinical development. The low volume of NER1006 is achieved through the use of ascorbate in the second dose only.

**Aims & Methods:** This phase 3, randomised, multicentre, colonoscopist-blinded, non-inferiority study assessed the efficacy, safety and tolerability of NER1006, administered either as a 2-day overnight (N2D) or 1-day morning (N1D) split-dosing regimen versus a 2 L PEG3350 with ascorbate 2-day overnight split dosing regimen (2LPEG) in patients undergoing a colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing efficacy and 'Excellent plus Good' cleansing rate in the colon ascendens using the Harefield Cleansing Scale (HCS). Secondary endpoints included hierarchical evaluation of lesion detection rates (key), and cleansing assessment using the Boston Bowel Preparation Scale (BBPS; supportive). Patient tolerability, acceptability and compliance were assessed using questionnaires. Safety was monitored through adverse events and clinical laboratory evaluation. The threshold for statistical significance in this study was $P<0.025$ and a 10% margin was used to demonstrate non-inferiority vs. 2LPEG.

**Results:** Patients ($n=283$/group) were randomised to receive N2D, N1D, or 2LPEG. Each respective group had a mean age (SD) of 56.3 (12.03), 54.9 (13.21) and 54.3 (12.48) years, and 120 (42.4%), 131 (46.3%) and 144 (50.9%) males. A high successful overall bowel cleansing efficacy was achieved in all three treatment groups (Table 1). N2D and N1D demonstrated non-inferiority to 2LPEG in overall bowel cleansing efficacy. N2D and N1D showed non-inferiority and superiority vs. 2LPEG in the 'Excellent plus Good' cleansing of the colon ascendens. Both N2D and N1D were non inferior to 2LPEG in detecting adenomas and polyps in the colon ascendens and in the overall colon (Table 1). In addition, N2D showed superiority for polyp detection in the colon ascendens. There were no deaths. NER1006 was not associated with any serious treatment-emergent adverse events (TEAEs). The most frequently reported related TEAEs for NER1006 were nausea and vomiting; and for 2LPEG, nausea and abdominal pain. Compliance levels were high in all treatment groups.

**Conclusion:** When administered as either a 2-day overnight or 1-day morning split-dosing regimen, and compared with 2LPEG, NER1006 was non-inferior in overall bowel cleansing success and lesion detection. It demonstrated a superior 'Excellent plus Good' cleansing rate in the colon ascendens. The 2-day NER1006 demonstrated a superior polyp detection rate in the colon ascendens. The overall tolerability and safety profile of NER1006 was comparable to that of 2LPEG; most TEAEs were mild or moderate in severity and reflected the expected safety profile of the respective treatments. The 1 L NER1006 showed high efficacy and safety in overnight or morning split-dosing administration.

**Disclosure of Interest:** R. Bisschops: Norgine, Self: Salary, Speaking and Teaching.
J. Manning: Funded attendance by Norgine for Investigator's Meeting trip for the MORA trial.
L.B. Clayton: Employee of Norgine.
R. Ng Kwet Shing: Employee of Norgine.
All other authors have declared no conflicts of interest.

**Abstract No: P0179**
**Table 1:** Efficacy and safety endpoints.

| Abstract legend<br>EFFICACY | NER1006 2-day split-dosing N2D Primary analysis set, n = 275 | NER1006 1-day split-dosing N1D Primary analysis set, n = 275 | Comparator: 2 L PEG3350 with Asc 2LPEG Primary analysis set, n = 272 | Confidence interval (CI) for the difference [P value] | |
|---|---|---|---|---|---|
| | | | | N2D vs. 2LPEG | N1D vs. 2LPEG |
| Primary endpoint: Patients with successful overall bowel cleansing efficacy (HCS) [n] | 253 (92.0%) | 245 (89.1%) | 238 (87.5%) | -4.00%* [0.055] | -6.91%* [0.328] |
| Supportive secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n] | 249 (90.5%) | 243 (88.4%) | 232 (85.3%) | n.a. | n.a. |
| Primary endpoint: Excellent plus Good cleansing rate in colon ascendens (primary analysis set) [n] | 87 (31.6%) | 93 (33.8%) | 41 (15.1%) | 8.11%* [<0.001] | 10.32%* [<0.001] |
| Key secondary endpoint: Adenoma detection rate, colon ascendens | 11.6% | 11.6% | 8.1% | -4.80%; 12.00%** [0.106] | -4.80%; 12.00%** [0.106] |
| Key secondary endpoint: Adenoma detection rate, overall colon | 26.6% | 27.6% | 26.8% | -8.47%; 8.02%** [0.569] | -7.65%; 9.11%** [0.455] |
| Key secondary endpoint: Polyp detection rate, colon ascendens | 23.3% | 18.6% | 16.2% | -1.41%; 15.47%** [0.024] | -6.12%; 10.82%** [0.268] |
| Key secondary endpoint: Polyp detection rate, overall colon | 44.0% | 45.1% | 44.5% | -8.85%; 8.00%** [0.579] | –7.78%; 9.09%** [0.478] |
| Compliance rates (min 75% of both doses taken) [n] | 235 (85.5%) | 233 (84.7%) | 245 (90.1%) | n.a. | n.a. |
| **SAFETY** | **Safety set, n = 262** | **Safety set, n = 269** | **Safety set, n = 263** | | |
| All treatment-emergent adverse events [n] | 77 | 89 | 53 | n.a. | n.a. |
| Patients with any related treatment-emergent adverse event [n] | 30 (11.5%) | 40 (14.9%) | 20 (7.6%) | n.a. | n.a. |

* = 97.5% 1-sided CI; ** = 95% 2-sided CI; n.a. = not applicable.

## P0180 COMBINATION ENDOSCOPIC THERAPY USING ENDOSPONGE AND OVER-THE-SCOPE-CLIP TO TREAT LARGE ENDOLUMINAL GI DEFECTS WITH INTRA-PERITONEAL OR THORACIC ABSCESSES

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**Introduction:** Management of large gastrointestinal fistulae and perforations is challenging and usually mandates surgery. Novel endoscopic closure methods have increased our ability to successfully occlude endoluminal GI defects. Nonetheless, there still exist situations where the defects are too large to allow for a one-step endoscopic closure. Sponge has been reported to be useful for closure of anastomotic fistulae.
**Aims & Methods:** The aim of this study was to evaluate the success, safety and complications rates of a multi-modal endoscopic approach using sponge, overt-the-scope clips to close large endoluminal GI defects. This is a retrospective, observational cohort study at a single academic institution during an 18-months period evaluating patients with severe and complex of large GI defects. The following over-the-scope clips were used preferentially 12/6 t and 12/6gc. The sponge was cut, sized and then attached to nasogastric or enteric tubes using Nylon 2–0. The tube-sponge device was then introduced into the GI lumen using overtubes of various sizes and lengths, depending on the location of the fistulae.
**Results:** During the study period we treated a total of 11 patients (8 male, 3 female, mean age 57.2 years; range 38 to 73) with large fistulae or perforations. The mean ASA socre was 3.5, range 3–4. Seven patients were critically ill at the time of consultation, with large perforation or intrabadominal abscess. The etiology of the GI defects involving the esophagus (n = 3), stomach (n = 3), small bowel N = 2) and colon (n = 3) were Boerhaave's syndrome n = 2, leak after gastric sleeve n = 2, colorectal anastomotic leak n = 2, lung abscess with tracheoesophageal fistula (n = 1), combined retroperitoneal and pleural abscess (n = 1), enterocutaneous fistula in Crohn's (n = 1), radiation-induced rectovesical fistula (n = 1). The defects were treated sequentially by endoscopic lavage and debridement, followed by insertion of sponge. Once the cavity decreased in size the sponge was exchanged or removed and the smaller diameter defect was closed using one or more over-the-scope clips. In defects larger than 5 cm a stent was also inserted to bridge the lumen. Five patients also underwent placement of a direct endoscopic jejunostomy using balloon-assisted enteroscopy technique. The mean number of procedures was 3, range 2–5. Successful closure of the GI defect and resolution of the abscess was achieved in six patients (54.4%). In three patients closure failed and they underwent surgery. Two patients died from underlying sepsis without improvement of their fistula. There were no adverse events related to the multi-modal endoscopic therapy.
**Conclusion:** The use of multi-modal endoscopic therapy based on endo-sponge and over-the-scope clip appears promising for the treatment of complex GI endoluminal defects, especially when patients are poor surgical candidates and are critically ill. In up to 50% of patients the therapy was successful, suggesting that this approach should be added to the armamentarium of the advanced endoscopist. Endoscopic interventions resulted in resolution of the bariatric complication in 50% of patients, therefore representing a valid alternative to treat these complications. However, some luminal defects associated with these types of surgery are recalcitrant to endoscopic approaches and require definitive surgical intervention to solve the problem. Nevertheless, endoscopy can serve as a bridge to surgery, thus decreasing the size of GI defect and improving the patient's general status.
**Disclosure of Interest:** K. Mönkemüller: Honoraria for lectures/teaching: Cook Medical USA, Ovesco, Tuebingen, Germany.
All other authors have declared no conflicts of interest.

## P0181 HIGH COMPLETE RESECTION RATE FOR PRE LIFT AND COLD BIOPSY OF DIMINUTIVE COLORECTAL POLYPS

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**Introduction:** The majority of polyps removed at colonoscopy are diminutive (≤5 mm) to small (≤10 mm) and there is no consensus method and limited data for the best way for these polyps to be removed.
**Aims & Methods:** We aimed to assess the effectiveness of cold biopsy forceps polypectomy with pre-lift (CBPP) for polyps ≤7 mm. Our aims were to assess completeness of histological resection of this technique, to identify factors contributing to this and assess secondary considerations such as timing, retrieval and complication rates. We conducted a prospective cohort study on consecutive patients receiving a colonoscopy on the British Bowel Cancer Screening program within the Gloucestershire National Heath Service Trust Hospital, Cheltenham General Hospital. Polyps were included if they were ≤7 mm and deemed appropriate by the colonoscopist. A maximum of 3 polyps per patient could be included for analysis. A small pre lift was used prior to complete visual removal of the polyp using cold biopsy forceps. The resected polyp was sent for standard histopathological assessment. The polypectomy site was then removed using endomucosal resection (EMR) with a margin of at least 1–2 mm. This was sent for histopathological analysis to assess completeness of resection. Polypectomy timing, tissue retrieval, number of bites required for visual resection and complications were recorded at the time of the procedure. Basic patient characteristics, colonoscopy indication, procedure time and withdrawal time were recorded.
**Results:** 64 patients were recruited and consented. Of these 42 patients had a total of 60 polyps that were included for pathological analysis after CBPP. Retrieval

was complete for all 60 polyps and there were no complications both during and after polypectomy. Three polyps were excluded from final analysis as they were inflammatory or post inflammatory polyps. Basic patient characteristics were similar in groups with and without polyps included in the study. Procedural times (36.04 vs 26.05 minutes) ($p = 0.01$) and withdrawal (25.36 vs 15.33) ($p = 0.002$) were significantly longer in those patients that had polyps included in the study. Overall CRR of polyps was 86%. Histology, polyp size, number of bites and location of resection did not significantly affect CRR and is summarised in Table 1.

**Table 1:** Complete resection rates (CRR) based on polyp characteristics.

| | Complete resection rate n/N (%) | 95% CI | P value |
|---|---|---|---|
| Overall complete resection | 49/57 (86) | 75–93 | |
| **Histology** | | | |
| Hyperplastic | 14/17 (82.4) | 60–95 | 0.61 |
| Adenomatous | 35/40 (87.5) | 75–95 | |
| **Size (mm)** | | | |
| ≤3 | 19/21 (90.5) | 73–98 | 0.26 |
| 4-5 | 14/15 (93.3) | 74–99 | |
| 6-7 | 16/21 (76.2) | 55–91 | |
| **No of bites** | | | |
| 1 | 25/30 (83.3) | 67–94 | 0.57 |
| 2-3 | 21/23 (91.3) | 75–99 | |
| ≥4 | 3/4 (75) | 27–98 | |
| **Location** | | | |
| Right colon | 20/23 (87) | 69–97 | 0.86 |
| Left colon (except rectum) | 20/24 (83.3) | 65–95 | |
| Rectum | 9/10 (90) | 63–99 | |

**Conclusion:** CBPP appears highly effective for polyps ≤5 mm with CRR >90% and a 100% retrival rate with no complications. Further studies are required to determine the optimal technique for complete histological resection of diminutive and small polyps.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0182 ASSESSMENT OF THE PATIENTS' PERCEPTIONS AFTER AN OUTPATIENT COLONOSCOPY AND THE QUALITY PROCEDURE

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**Introduction:** In the Basque Country (one of the 17 autonomous regions in Spain), with an approximate population of 2, 200, 000 inhabitants, colorectal cancer (CRC) screening—by immunochemical test (FIT) and colonoscopy under sedation as a diagnostic procedure—was introduced in 2009. Since then, the quality of the colonoscopies performed—regardless of what the reasons for the colonoscopy have been (screening/diagnostic)—has been improving by following the European and Spanish Guidelines and the continuous evaluation of the process and results. However, more than 30, 000 colonoscopies are carried out by the public health service every year and we do not know what the patient's perceptions are at the different stages of the process, disregarding the results of the procedure related to quality criteria.
**Aims & Methods:** To obtain information regarding the perceptions of the patients after a colonoscopy and to compare them with the quality indicators of the procedure based on the European Guidelines of quality assurance on colorectal cancer screening and diagnosis. Cross-sectional study. 1) Design and validation of a survey which includes questions to be asked previous to, during and after the colonoscopy. Aspects covered: waiting time, cleansing method, information provided, discomfort/pain previous, during and after the procedure, attention and global satisfaction. 2) Stratified by 12 different colonoscopy units, depending on the annual volume of colonoscopies. 3) Target population: men and women 40–75 years old, who have had a colonoscopy 24–48 hours previous to the interview. 4) All interviews were done by two trained interviewers via telephone calls and recorded after the patient gave her/his informed consent. 5) Period: November- December 2015. 6) All data related to each colonoscopy were registered including: cleansing, sedation, lesions found, tolerance and adverse effects.
**Results:** 90.8% of the 445 people selected for the sample accepted to take part in the survey. 52.0% were men and 45.6% were less than 60 years old. The main reason to perform the colonoscopy was by symptoms (33.3%), followed by screening (30.6%) with sex differences ($p = 0.02$). Waiting time was less than 30 days in 52.4% of the cases, considered too long by the 19.6% of participants. 89.7% received instructions—offered by primary-care physician or nurse (94.2%)—previous to the colonoscopy and these were considered appropriate by 87.0% of the patients. 80.3% of the cases had an adequate colonic cleansing, but more fasting hours had a significant impact on poor colonic cleansing. In 78.2% of the cases, deep sedation was registered, however only 21 patients reported pain. In 231 (51.9%) cases polyps or CRC were detected. No severe or fatal complications occurred. Global satisfaction score was above 8 (1 to 10 scale), 81.6% disregarding waiting time or pain.
**Conclusion:** The assessment of our patients' perceptions is a very useful tool to improve information to give them, as well as the colonoscopy report. Even though the global satisfaction score was high, waiting time, levels of pain, cleansing methods and the quality of the information provided during all the process should be improved.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0183 COLD SNARING POLYPECTOMY IS A BETTER PROCEDURE FOR RESECTING THE DIMINUTIVE COLON POLYP

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**Introduction:** Clinically, cold forceps polypectomy (CFP) may be more popular procedure for resecting the diminutive colon polyp because of the simplicity. However, there remain problems of CFP in regards to the piecemeal resection or a snare cost for resecting the other larger polyps in the same examination, while cold snaring polypectomy (CSP) enables resection for the small-to-large lesions (<10 mm).
**Aims & Methods:** To verify the usefulness of CSP for treatment of the diminutive polyps (<4 mm) compared to CFP, consecutive patients who underwent cold polypectomy (CP) in Omori Red Cross Hospital from 2015 January to 2015 December were retrospectively analyzed. We used 10 mm Captivator TM[II] for CSP and Radial Jaw[TM] 4 Jumbo for CFP (Boston scientific). These patients were divided in 2 groups; patients resected by CSP and patients resected by CFP. We use clips for cases with immediate bleeding or delayed bleeding more than 2 minutes after procedure. Two groups were compared with relative to the medication, tumor characteristics, the rate of complete en bloc resection and complication.
**Results:** 235 patients underwent CP; 98 patients with 175 lesions (CSP group) and 137 patients with 190 lesions (CFP group). Anticoaglant patients were 17 cases (17.3%) in CSP group and 17 cases (12.4%) in CFP group. In addition, 6 cases (35.3%) in CSP group and 8 cases (47.1%) in CFP group underwent CP without cessation of anticoaglant agents. The tumor shape (Is : Isp : Ip : IIa) was 60 : 9 : 1 : 105 in CFP group and 63 : 4 : 0 : 123 in CSP group, respectively. The rate of using clips was similar between two groups (7.4% in CSP, 3.2% in CFP). The rate of piecemeal resection in CFP group (7cases, 3.7%) was significantly higher than that of CSP group (0%) ($p = 0.010$). Cases with poor resected specimen (positive or unclear of tumor margin) in CFP group (70, 36.8%) were more than that of CSP group (46, 26.3%) ($p = 0.033$). There was no difference in complication, such as post-bleeding or perforation, between two groups (0% vs 0%).
**Conclusion:** With regards to completeness of resection or safety in CP of diminutive polyps, CSP performed better. It is difficult to predict what kind of polyps will be detected during the colonoscopy, so CSP will be a better way for treating diminutive polyps.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0184 THE ROLE OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN EARLY-STAGE LOWER RECTAL TUMOUR TREATMENT

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**Introduction:** The operative method for early stage lower rectal cancer must be selected carefully from the perspective of functional preservation. Compared with other operative techniques, endoscopic resection, especially endoscopic submucosal dissection (ESD), is a minimally invasive treatment that has a high curability rate and using which, surgical resection may be avoided. Therefore, it is also relevant for diagnostic treatment. Furthermore, ESD is considered an effective treatment for lesions close to the anal canal, residual recurrent lesions (after EMR and TEM), and large lesions (≥5 cm), which were considered difficult to resect using traditional endoscopic treatments (Endoscopic mucosal resection:EMR). Therefore, we examined the effectiveness of ESD.

**Aims & Methods:** Of the 67 patients with lower rectal lesions treated with ESD at our hospital we selected patients with: (1) lesions close to the anal canal (17 lesions), (2) residual recurrent and lesions with scaring (eight lesions), and (3) large lesions (≥5 cm) (22 lesions). We examined tumour size, operation time, en bloc resection rate, and accidental symptoms.
**Results:** (1) The size of tumour was 53.7 mm (range 12–150 mm), mean operation time was 96.6 minutes (range 15–250 minutes), curative resection rate was 94.1%, and complication included one postoperative bleeding and one stenosis. (2) The mean tumour size was 45.1 mm (range 10–100 mm), mean operation time was 93.4 minutes (range 15–250 minutes), curative resection rate was 87.5%, and no procedural accident was registered. (3) The size of tumouur was 85.8 mm (range 50–175 mm), mean operation time was 97.9 minutes (range 50–240 minutes), and curative resection rate was 81.8%; procedural accidents included two cases of postoperative bleeding and one of stenosis. En bloc resection was possible in all cases, without residual stenosis.
**Conclusion:** We demonstrated that ESD could give favourable results for lesions that were conventionally treated surgically because of endoscopic treatment difficulties. Surgical treatment could be predominantly invasive and associated with dysfunction, but with ESD, lesions could be resected with complete functional preservation. Therefore, ESD can be considered an effective, non-invasive treatment option, even for lesions that are difficult to treat with traditional endoscopic treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0185 METAL OR PLASTIC STENTS TO RELIEVE OBSTRUCTIVE JAUNDICE PRIOR TO RESECTION OF PERIAMPULLARY TUMORS RESULTS OF A PROSPECTIVE RANDOMIZED, DOUBLE BLIND CLINICAL STUDY

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**Introduction:** Albeit that preoperative biliary drainage prior to pancreaticoduodenectomy has been questioned, it remains controversial and clinically most relevant, not the least in light of the emergence of novel therapeutic concepts in the form of neoadjuvant therapies. Therefore we embarked on a randomized clinical study to compare preoperative stenting by use of conventional plastic vs modern self expandable metal (SEMS) stents.
**Aims & Methods:** The sample size estimate of the study was based on a difference in enteric bacterial colonization of intrahepatic bile at the time of resection as a marker of the efficacy of the bile drainage executed by the respective stent type. 92 patients were randomized with 45 allocated to a plastic stent and 47 received a SEMS. Although all patients were originally considered to be eligible for a curative resection, eventually only 59 were found to be suitable for a resection with curative intent. Of these were 32 originally allocated to the plastic stent group and 27 to the SEMS group. Whenever a potential stent dysfunction appeared the patient remained in the originally allocated group even if replacement of the stent was required. Until the time of resection or change of stent, the group affiliation was blinded for the patient as well as the assessor.
**Results:** The patients were well matched regarding clinical and disease-specific characteristics. During the preoperative biliary drainage period more stent dysfunctions requiring stent-exchanges were recorded in the plastic stent group (19% vs 0%, $p < 0.05$). At the time of the operation we were unable to detect any important differences in the macroscopic assessment of the region for stent deployment, nor concerning the microscopic scoring of the grade of inflammation. No differences could be visualized in the amount and composition of the bacterial cultures from the aspirated intrahepatic and gallbladder bile. However, postoperative complications were more frequent in patients being treated with plastic stents (72% vs 52%, $p = 0.11$) with a numerical difference in number of clinical significant leakages (12% vs 3.7%, $p = 0.36$).
**Conclusion:** The need for preoperative biliary drainage remains in light of current development of therapies for periampullary tumors. The results of the current randomized, clinical study offer strong arguments in favor of SEMS to minimize the ensuing postoperative risk profile.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0186 IMPACT OF DISCONNECTED PANCREATIC DUCT SYNDROME ON THE ENDOSCOPIC MANAGEMENT OF PANCREATIC FLUID COLLECTIONS

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**Introduction:** Disconnected pancreatic duct syndrome (DPDS) encountered in severe pancreatitis is characterized by complete transection of the main pancreatic duct (MPD) resulting in a variable portion of the upstream pancreatic gland becoming isolated from the MPD downstream. The upstream gland secretes pancreatic juice that results in a non-resolving percutaneous fistula or pancreatic fluid collection (PFC).
**Aims & Methods: Aim:** To study the impact of DPDS on the endoscopic management of PFCs. **Methods:** This is a retrospective study of patients undergoing endoscopic drainage of PFCs over 12-years (2003–2015). Initial treatment consisted of endoscopic or endoscopic ultrasound (EUS)-guided transmural stenting. If treatment response was suboptimal, multidisciplinary hybrid interventions included drainage by EUS-guided multi-gate technique, dual (endoscopic-radiology) modality technique and/or endoscopic/percutaneous sinus tract necrosectomy. While the transmural stents were removed after PFC resolution during the initial 5 years, they were left permanently in patients with DPDS in the later period. Main outcome measures were to evaluate the impact of DPDS on the need for hybrid treatment, re-interventions, rescue surgery, length of stay (LOS) and overall treatment success.
**Results:** Of 361 patients, 34 (9.4%) were acute collections, 178 (49.3%) pseudocysts and 149 (41.3%) walled-off necrosis (WON). DPDS was more frequent in WON compared to other PFC types (68.3% vs. 31.7%; $p < 0.001$). While there was no significant difference in overall treatment success (85 vs. 91.9%, $p = 0.07$), more DPDS patients required hybrid interventions (31.1 vs. 4.8%, $p < 0.001$), re-interventions (30 vs. 18.5%, $p = 0.03$), rescue surgery (13.2 vs. 4.8%, $p = 0.02$) and longer LOS (median days, 3 [2–10] vs. 2 [1–4], $p = 0.003$). PFC recurrence was significantly less in DPDS patients with permanent transmural stents (17.4 vs. 1.7%, $p = 0.001$). Multivariate logistic regression revealed that the presence of DPDS (OR 2.99, 95% CI 1.06–8.47, $p = 0.039$), WON (OR 3.37, 95%CI 1.41–8.06, $p = 0.006$) and multiple (OR 10.6, 95% CI 4.7–23.6, $p < 0.001$) or large (≥10 cm in size) PFCs (OR 2.66; 95% CI 1.19–5.95, $p = 0.017$) were associated with need for hybrid interventions.
**Conclusion:** DPDS has a significant impact on endoscopic management of PFCs as these patients require more multidisciplinary hybrid interventions for achieving optimal clinical outcomes.
**Disclosure of Interest:** R. Hawes: Consultant for Boston Scientific Corporation and Olympus America Inc.
S. Varadarajulu: Consultant for Boston Scientific Corporation and Olympus America Inc.
All other authors have declared no conflicts of interest.

Abstract No: P0188
Therapeutic Intent n = 137

| | Stones | Stent removal | Ablation | Stent access | Wire advancement | Success % |
|---|---|---|---|---|---|---|
| Extrahepatic | 106 | | | | | 106/106 (100) |
| Intrahepatic | 13 | 3 | 4 | 2 | 3 | 22/25 (88) |
| Cystic duct | 7 | | | | 1 | 8/8 (100) |
| **Diagnostic Intent n = 163** | | | | | | |
| Stricture n = 145 | Pre-SODC Suspected | Post-SODC confirmed | | | | |
| | Benign | Malignant | Benign | Malignant | | |
| PSC n = 20 | 19* | 1 | 19 | 1 | | |
| OLT n = 23 | 23 | 0 | 23 | 0 | | |
| Indeterminate n = 102 | 10 | 92 | 19 | 83 | | |
| Filling defect n = 6 | 5 | 1 | 1 | 5 | | |
| Dilated duct n = 9 | 9 | 0 | 7 | 2 | | |
| Hemobilia n = 3 | 1 | 2* | 1 | 2* | | |

## P0187 A NEW MODEL OF ACUTE OBSTRUCTIVE JAUNDICE MANAGEMENT IN THE EMERGENCY DEPARTMENT

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**Introduction:** Is it well known that obstructive jaundice is a frequent cause of access in Emergency Department (ED), with or without cholangitis, and this requires a rapid management with hospitalization in surgical or gastroenterology unit to perform ERCP and to solve the problem. To reduce the problem of overcrowding and too many hospital admissions in Italian EDs were added Brief Observation Unit (BOU), small units located close to the ED in which patients are treated for 48–72 h with a significant decrease of regular admission costs. Aim of our study was evaluate the efficacy of a new model of managing acute obstructive jaundice with ERCP procedures directly from BOU, instead of admitting patients to long and unnecessary periods of hospitalization.
**Aims & Methods:** We enrolled from July 2014 to November 2015, 172 consecutive patients (102 M/70F mean age 66.7 +- 13.5) who came to our ED of Gemelli Hospital with an acute obstructive jaundice with the indication to perform ERCP Routine blood tests including LFTs, chest x-ray, EKG, abdominal ultrasound (or CT scan if needed) were performed and the patient sent urgently to perform ERCP. After ERCP patients were hospitalized for a short observation in the BOU close to the ED in which patients are treated for 48–72 h with a significant decrease of regular admission costs. Aim of our study was evaluate the efficacy of a new model of managing acute obstructive jaundice with ERCP procedures directly from BOU, instead of admitting patients to long and unnecessary periods of hospitalization.
**Results:** Indications for ERCP are summarized in the table.

| | Patients | % of patients | % of discharge after observation |
|---|---|---|---|
| **Removal of bilary stones** | 98/172 | 57% | 71.4% |
| **Bilary Stent Clogging** | 34/172 | 19.8% | 94.1% |
| **Cholangitis with incomplete drainage from other facility** | 3/172 | 1.7% | 0% |
| **Unresectable Pancreatic cancer** | 35/172 | 20.3% | 85.7% |
| **Acute biliary pancreatitis** | 2/172 | 1.2% | 0% |

Overall, 132 / 172 patients (76.7%) were discharged the day after the procedure or within 48 hours from admission ($p < 0.0001$). Biliary stent clogging, unresectable pancreatic cancer and removal of biliary stones are the diseases in which treatment determined a significantly high probability of discharge directly form BOU, differently from cholangitis with incomplete drainage from other facilities or acute biliary pancreatitis, which always require regular hospital admission ($p < 0.0001$). This model allowed to significantly reduce the total costs of management of those diseases (291 vs 1058 USD per day for each patient; $p < 0.0001$).
**Conclusion:** Our study showed the effectiveness of BOU in the managing of patients with acute obstructive jaundice who needs ERCP, especially for those who underwent for removal of biliary stones or biliary stent clogging. All of these patients were admitted to BOU, thereby reducing the cost and time of hospitalization. This approach decreases unnecessary inpatient admission, reduces timing of procedures actuation and allows a faster and appropriate managing of the patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0188 SINGLE OPERATOR DIGITAL CHOLANGIOSCOPY (SODC): MULTICENTER EXPERIENCE IN 300 PATIENTS

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**Introduction:** Cholangioscopy for diagnostic and therapeutic purposes of bile duct disorders is important to confirm pathology, assess for disease extent and provide non-surgical therapies.
**Aims & Methods:** A multicenter retrospective review of 300 patients who had SODC performed with therapeutic intent (137) and diagnostic intent (163). A single-use, multi-purpose 10.5 Fr flexible endoscope, all-inclusive design with independent irrigation and a 1.3 mm therapeutic channel (SpyGlass DS$^{tm}$, Boston Scientific, MA, USA) was used in an outpatient setting under monitored anesthesia, all with prophylactic antibiotics and biliary sphincterotomy; Standard imaging findings, endoscopic findings, treatment and pathology were reviewed.
**Results:** (* 1 not biopsied) SODC modified the extent of biliary strictures in malignant strictures in 26/102 (25.4%), all with greater extent. Three patients with OLT stricture did not have a stricture but cast stones. Of the suspected malignant strictures, 1 had portal cholangiopathy, 4 AIC, 1 post-radiation, 1 ischemia, 12 inflammatory. Biopsy performed via SODC (SpyBite$^{tm}$, Boston Scientific, MA, USA) diagnosed cancer in 83 patients with strictures, EHD 34/40 (85%) and IHD 55/62 (90%). The visual appearance by DSOC suggested cancer in 86/102 (84.3%) and benign in 15/19 (79%). In patients with filling defects, a neoplastic process was diagnosed in 5, all suspected to have stones. The majority of patients with dilated bile duct had benign disease whereas the majority presenting with hemobilia had malignant disease. There were no complications noted attributable to DSOC except for one OLT patient with transient cholangitis.
**Conclusion:** DSOC is safe and effective permitting various therapies: it is highly effective in the management of stone disease and it is of significant value in diagnosing malignant lesions, distinguishing benign from malignant strictures secondarily altering diagnosis and prognosis.
**Disclosure of Interest:** I. RAIJMAN: Speaker and consultant, Boston Scientific Corporation Speaker, ConMed Speaker, Covidien Speaker, Takeda.
P. Tarnasky: Speaker and consultant, Boston Scientific Corporation.
R. Shah: Speaker and consultant, Boston Scientific Corporation.
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All other authors have declared no conflicts of interest.

## P0189 EXTERNAL VALIDATION OF THE EGSE'S CRITERIA ON DIFFICULT ENDOSCOPIC BILIARY CANNULATION: IDENTIFYING OPTIMAL TIMING FOR A RESCUE TECHNIQUE

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**Introduction:** The definition of ''difficult biliary cannulation'' was very heterogeneous in each study although it has been addressed by the European Society of Gastrointestinal Endoscopy (ESGE) in 2014 as any of the following factors: duration of >5 minutes, >5 attempts or >2 pancreatic guidewire passages.
**Aims & Methods:** The aim of this study was to validate the EGSE criteria and identify an optimal timing for rescue technique. Endoscopic retrograde cholangiopancreatography (ERCP) registry was prospectively maintained from November 2014 to December 2015 in six teaching hospitals, Daegu, South Korea. Decision tree analyses with CHAID (Chi-squared Automatic Interaction Detection) was conducted for external validation of the three factors (biliary access duration, attempt, pancreatic guidewire passage) for post-ERCP pancreatitis (PEP) and the cut-off time of switching to rescue biliary access technique.
**Results:** A total of 1, 067 consecutive patients with naïve papilla were included. Selective bile duct cannulation succeeded in 761 (70.4%) patients with first attempt. Overall success for the biliary cannulation was 1, 040 (97.4%) with median time of 5 minutes (range 0.5 – 59) and PEP occurred in 72 (6.7%) patients. In CHAID decision tree analyses, the duration of biliary cannulation was the most decisive factor, whereas the number of biliary attempt was not included in decision tree model. Furthermore, two cut-off times of biliary cannulation were identified, which were 2 minutes with 3.4% PEP and 5 minutes with 11.8% PEP.
**Conclusion:** The duration of biliary cannulation was the most decisive factor for PEP. And if the duration of biliary cannulation exceeds 5 minutes, the risk of PEP is expected to increase by up to 12%. Therefore, we suggest that 5 minutes could be the cut-off time for switching to other rescue technique.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0190 EVALUATION OF LEARNING CURVE FOR NEEDLE KNIFE PRECUT SPHINCTEROTOMY

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**Introduction:** Selective deep cannulation of the common bile duct (CBD) is a crucial step for successful endoscopic retrograde cholangiopancreatography (ERCP). Precut is a technique used when standard techniques fail. It is associated with higher rates of post-ERCP complications such as pancreatitis, bleeding and perforation. These have been reported to be as high as 12–22%. There is currently no consensus on what constitutes adequate training for precut. Moreover, no studies have defined the minimum threshold needed to achieve basic competency. It is therefore relevant to examine the learning curve in precut to optimize training outcomes and patient safety.
**Aims & Methods:** Aim: To determine the number of procedures required before effective and safe precut sphincterotomy can be achieved. Methods: Retrospective observational study of efficacy and safety of needle knife precut sphincterotomy to achieve selective deep CBD cannulation. Data of all patients who underwent ERCP by an experienced Endoscopist in a tertiary centre were reviewed. These data have been maintained in a prospective registry established for quality control. All patients who underwent needle knife precut during ERCP were included. Patient demographics, co-morbidities, ASA status, indication for ERCP, success rate of index precut and complications were recorded. Success was defined as successful selective deep CBD cannulation after precut. Success rate was analysed as a function of number of procedures performed. The minimum acceptable success rate was arbitrarily predefined as 85%, as this is the rate of successful CBD cannulation achievable by most Endoscopists. We predefined a more stringent acceptable threshold for developing a complication as 10% or less in our study.
**Results:** 158 patients underwent needle knife precut sphincterotomy from December 2005 to October 2015 (male 55.1%; mean age 66.2 ± 15.8 years). Commonest indications were cholangitis and obstructive jaundice (61/158, 38.6% and 73/158, 46.2% respectively). 140/158 (88.6%) had ASA scores 2 or less, with the remaining patients having an ASA score of 3. 141/158 (89.2%) patients had a successful index ERCP. The number of procedures to achieve a probability of success of 85% was 6. A success rate of 85% and above was maintained consistently after 13 precut procedures. The exact one-sided binomial test showed that the probability of a successful precut was not statistically higher than the threshold of 85% for the first one hundred precuts. At the 125th precut, the probability of successful index ERCP was significantly higher (91%; $p = 0.029$) than the predefined threshold. However, this became insignificant at the 150th precut performed. 2/158 (1.3%) patients developed bleeding and 5/158 (3.2%) patients had pancreatitis after precut. The risk of pancreatitis was 2.0% after the 50th precut, which was significantly lower than the 10% predefined threshold ($p = 0.034$). For bleeding, the probability of developing this complication was 3.0% at the 75th precut, which was significantly lower than the 10% threshold ($p = 0.016$). Both complication rates were well-maintained below 5.0% beyond the 50th precut performed, with bleeding rates showing a continual decline to 1% at the 150th precut, while pancreatitis rates remained relatively constant between 2.0% to 4.0%. There were no patients with perforation in our study.
**Conclusion:** An experienced Endoscopist requires at least 13 precut procedures to achieve a sustained success rate of 85% or more. Significant improvements in complications below a predefined 10% threshold were achieved after 50 and 75 precuts for pancreatitis and bleeding respectively. Bleeding rates continue to improve beyond this point, but pancreatitis rates remained relatively constant.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0191 EFFICACY AND SAFETY OF DILATION-ASSISTED STONE EXTRACTION (DASE) PLUS SPHINCTEROTOMY (EST) IN PATIENTS WITH COMMON BILE DUCT LARGE STONES: A RETROSPECTIVE MULTICENTER STUDY

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**Introduction:** The endoscopic treatment of bile duct stones is commonly performed worldwide and has a success rate of 90%. Endoscopic sphincterotomy (EST) is the standard method for enlarging the common bile duct (CBD) opening in the duodenum before stone removal during endoscopic retrograde cholangiopancreatography (ERCP). However, approximately 10–15% of patients present with bile duct stones that are difficult to remove using standard techniques for large or impacted stones or for stone located proximal to biliary structures. There may be technical difficulties related to peri-ampullary diverticulum, coagulopathy or Billroth II gastrectomy. Recently, Dilation Assisted Stone Extraction (DASE) alone or plus EST has been reported as another alternative technique that is more efficient than EST alone for removal of CBD stones.
**Aims & Methods:** We collected and analysed data on 194 patients from 5 centres who underwent DASE (194/3150 of all ERCP done for stone [15%]) from Jan 2013 to Dec 2015 for the treatment of common (large) bile duct stones. All patients had undergone EST**.** Some patients underwent to DASE directly, others after failure of removal stones with standard technique (basket or retrieval balloon). Cannulation of CBD took place by contrast-assisted or wireguide-assisted techniques or after papillary pre-cut. The guidewire was maintained in the CBD while diagnostic catheter was removed and exchanged with dilating balloon catheter. The dilating balloon was advanced over the guidewire and positioned in the mid-portion of the balloon across the major duodenal papilla. The balloon was then inflated gradually with diluted contrast and maintained for 30–60 sec in situ. The size of the balloon was 10–20 mm in diameter according to the diameter of the CBD. Stone extraction after DASE was performed with either stone retrieval baskets or balloon-tipped catheters.
**Results:** 110/194 pts were females (57%), with a mean age of 70.5 (SD 14.9) yrs; 69 pts (39%) had previous EST (minimal sphinterotomy in 46%, 54 (28%) periampullary diverticulum and 8 pts (4%) Billroth II gastrectomy. The wire-guide-assisted technique was used in 90%, pre-cut in 8% and contrast-assisted techniques in 2%. DASE was used as first approach in 69% and after initial failure to remove stone with standard techniques in 31%. The indication for DASE were large stones (78%), intra-diverticular papilla (22%) or coagulopathy just in one patient. DASE was used mainly as an elective (95%) procedure. Technical success (complete dilation) was reached in 94% of patients. The mean final dilation was 15 (±3.7) mm in diameter. In 183 patients (94%) stones were successful removed from the CBD (50% with retrieval balloon and 50% with Basket). Twenty-seven complications (13.9%) occurred: 15 bleeding

**Abstract No: P0192**
**Table:** Variables of inflammation/activity in relation to bile duct enhancement in MRI.

| | MRI BILIARY ENHANCEMENT IH | | MRI BILIARY ENHANCEMENT EH | |
|---|---|---|---|---|
| | <2 mm | >2 mm | <2 mm | >2 mm |
| ALP, UI/L | #14 204 (138-447) | #30 214 (145-370) | #14 184 (154-320) | #34 227 (111-383) |
| GGT, UI/L | #14 331 (122-472) | #30 203 (106-360) | #14 291 (122-291) | #34 223 (65-364) |
| ALT, UI/L | #14 191 (31-226) | #30 67 (32-123) | #14 38 (24-212) | #34 64 (34-139) |
| AST, UI/L | #14 96 (33-120) | #30 58 (37-104) | #14 43 (31-111) | #34 60 (37-101) |
| Ca19-9, kU/L | #14 6 (2-9)* | #30 12 (5-49)* | #14 9 (2-15) | #34 9 (7-32) |
| CEA, ng/mL | #14 1.5 (0.7–1.9) | #30 1.1 (1-2.7) | #14 1.4 (1–1.9) | #34 1.2 (1-2.7) |
| Biliary Calprotectin, mg/L | #5 11 (4-470) | #15 35 (1-149) | #6 7.8 (1-292) | #17 32 (1-158) |
| Biliary Lymphocytes 0 1 2 | #12 25% 75% 0% | #27 7% 93% 0% | #13 15% 85% 0% | #30 10% 87% 3% |
| Biliary Neutrophils 0 1 2 | #12 17% 50% 33% | #27 7% 63% 30% | #13 8% 61% 31% | #30 13% 53% 34% |
| Intraepithelial inflammation 0 1 | #12 33% 67% | #27 33% 67% | #13 46% 54% | #30 33% 67% |
| Papanicolau classification 1 2 3 4 | #12 17% 67% 17% 0% | #27 4% 78% 11% 7% | #13 8% 84% 8% 0% | #30 7% 73% 13% 7% |

#number of patients tested. *p = 0.028; all other variables not significant. Neutrophils, lymphocytes: 0 = absent, 1 = mild, 2 = high. Intra-epithelial inflammation: 0 = absent, 1 = present Cytology classification (Papanicolaou): 0 = no neoplasia, 1 = bening atypia, 2 = mild suspicion of neoplasia, 3 = high suspicion of neoplasia

episodes, 11 pancreatitis and 1 perforation. The majority of these complications were immediate (44%) or occurred within 24 hours (41%). Only one patient died, because of perforation despite surgical treatment. The pancreatitis prophylaxis was done by using in majority rectal indomethacin (58%) or with stent placement (9%).
**Conclusion:** Dilation Assisted Stone Extraction after EST is safe and effective in treatment of large CBD stones and might be useful in patients who have a high risk of complications associated with extensive sphincterotomy, such as diverticula or bleeding tendencies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0192 CORRELATION OF MAGNETIC RESONANCE IMAGING WITH MARKERS OF DISEASE ACTIVITY AND PROGRESSION IN PRIMARY SCLEROSING CHOLANGITIS

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**Introduction:** Primary sclerosing cholangitis (PSC) is a cholestatic chronic liver disease, associated with an increased risk of biliary dysplasia and carcinoma. Alkaline phosphatase (ALP) has been used as a marker of disease activity and progression[1], but more reliable and validated surrogate markers are needed[2]. The role of magnetic resonance imaging (MRI) and bile duct enhancement in predicting disease activity and dysplastic changes in PSC is still unclear.
**Aims & Methods:** The aim of the study was to investigate the role of MRI and biliary enhancement as a non-invasive marker of disease activity in PSC in a group of patients, who systematically underwent endoscopic retrograde cholangiography (ERC) surveillance with brush cytology and bile collection. PSC diagnosis was based on patient's history, laboratory tests, histology, cholangiographic findings and clinical follow-up. All PSC patients who underwent MRI and ERC within 3-month interval (n = 50) were retrospectively collected from PSC register of our hospital (n = 614). MRI images were reviewed by two radiologists and biliary enhancement was categorised in <2 mm and >2 mm for intra- and extra-hepatic (IH and EH) bile ducts. Serum ALP, gamma-glutamyl transpeptidase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (Ca19-9) as well as biliary concentration of calprotectin were collected, when available. Brush cytology was reviewed by pathologist for inflammation and dysplasia classification (Table). Categorical and continuous variables were expressed as percentage and median (25%– 75%), respectively. Differences between enhancement and variables were tested with the Fisher's Exact Test and with the Mann Whitney test, when appropriate.
**Results:** Overall, 61 MRI (1.5 Tesla in 51 and 3 Tesla in 10; 3D in 58) and ERC have been performed (14 for diagnosis and 47 for follow-up) in 50 PSC patients (male 38, median age at diagnosis 31; 6–75, median age at MRI/ERC 38; 15–75) and included in the analysis. Table shows variables' distribution according with the different biliary enhancement. A significant difference was found only in Ca19-9 values between MRI biliary enhancement groups in IH (p = 0.028), but not for any other variables.
**Conclusion:** Although MRI is an accurate, cost-effective and non-invasive procedure for diagnosis and follow-up of PSC, its role as an accurate surrogate marker for biliary inflammation and dysplasia seems to be limited.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0193 MANAGEMENT OF BILIARY ANASTOMOTIC STRICTURES AFTER LIVER TRANSPLANTATION (BASALT STUDY): A NATIONWIDE ITALIAN SURVEY

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**Introduction:** Management of biliary anastomotic strictures (AS) after liver transplantation remains to be defined.
**Aims & Methods:** To retrospectively report the endotherapy workload for AS and its management in Italy, a questionnaire was sent to the Endoscopy Units of Italian Liver Transplantation Centers.
**Results:** Nineteen of the total 21 Units (90%) returned the questionnaire, twelve being high-volume (>250 ERCPs/year) Units. During 2013, 248 liver-transplanted (LT) patients underwent AS endotherapy and 560 (7.3%) out of 7, 679 ERCPs (median/Center 16, range 5–204) were performed for AS. After unsuccessful ERCP, interventional radiology or surgery was used in 6% and 3.2% of patients, respectively. The ERCP selection criteria included the trend of liver tests in 84% of the Units, associated with AS as documented by non-invasive imaging in 89%. AS was treated by fully covered self expandable metal stent (SEMS) or plastic multistenting (PM) in eight Centers, only by PM in ten and by single plastic stenting in one. SEMS was used independently of the overall ERCP workload and removed after three (37%) or six (63%) months. PM was planned at three-month intervals or at stent dysfunction in 94% of the Units. The duration of endotherapy was planned up to the radiological resolution of the stricture in most Centers. Recurrent AS was treated endoscopically in 79% of Centers, by PM in most Units and by fully covered SEMS in 5%.
**Conclusion:** In Italy endotherapy is confirmed as the preferred first and second-line management option for AS and progressive plastic multi-stenting is most frequently used.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0194 COMPARISON OF ERCP SUCCESS RATE IN EST-NAÏVE PATIENTS WITH ADVANCED AND NON-ADVANCED LIVER CIRRHOSIS

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**Introduction:** Although endoscopic retrograde cholangiopancreatography (ERCP) is one of the standard pancreatobiliary interventional methods, there is limited study about ERCP in patients with liver cirrhosis. The aim of this study is to assess the ERCP success rate in endoscopic sphincterotmy (EST)-naïve patients with cirrhosis.
**Aims & Methods:** In a single tertiary teaching hospital, total 135 EST-naïve patients with cirrhosis who had undergone ERCP were identified between 2003 and 2015. The ERCP success was defined with successful deep cannulation with drainage or stone removal. Advanced liver cirrhosis was defined as Child-Pugh-Turcot classification (CPT) C.
**Results:** Proportion of male sex was 71.1 (%) and median age was 62 years. Major causes of ERCP were CBD stone (60.7%), malignant biliary obstruction (24.4%), and others (14.8%). According to CPT A, B, and C, number of patients was 33, 67 and 35, respectively. The initial ERCP success rates of each group were 93.9%, 94.0% and 80.0%, which showed lower success rate in CPT C group. (P = 0.001). However, success rates increased to 97.0%, 98.5%, and 91.4% after the repeated ERCP trial. As a result, the eventual success rates between non-advanced (97.9%) and advanced group (91.4%) were not statistically different (P = 0.132).
**Conclusion:** Compared with patient with CPT A and B, there is a significant lower success rate of initial ERCP in patients with CPT C. However, there is no difference in final success rates including re-trial of ERCP. ERCP in patients with advanced cirrhosis is feasible with a proper preparation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0195 EFFICACY AND SAFETY OF LEFT LATERAL POSITION FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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**Introduction:** Endoscopic retrograde cholangiopancreatography (ERCP) has been widely used in diagnosis and treatment of pancreaticobiliary diseases. ERCP has been usually performed in the prone position. The prone position for ERCP can facilitate selective bile duct cannulation, offer a better fluoroscopic image of pancreaticobiliary anatomy, and prevent aspiration of gastric contents. However, in cases of difficulty in the prone position, ERCP can be performed in the left lateral position. Compared with the prone position, left lateral position is more comfortable for patients, especially with limitation for cervical movement including cervical cord injury, cervical spine operation, parkinson's disease, muscle contracture due to cerebral infarction, and allow more easy passage of the scope through the pharynx, and useful to secure airway.
**Aims & Methods:** We aimed to evaluate the efficacy and safety of left lateral position for ERCP compared with prone position in this prospective, controlled study. Between August 2015 and March 2016, a total 62 patients with naïve papilla who underwent ERCP at Hallym University Chuncheon Sacred Heart Hospital in Korea, were enrolled. They were randomly assigned to the left lateral position (n = 31) and the prone position (n = 31) before procedure. Age, sex, indication for ERCP, comorbidity, anticoagulation agent, American Society of Anesthesiologists (ASA) class, dose of sedative agent, dose of analgesics, procedure time, type of periampullary diverticulum, pancreatic duct cannulation, acquisition of pancreatogram, need of precut, type of papillary sphincter therapy, success of procedure, and adverse event including pancreatitis, bleeding, infection, cardiopulmonary complication, basket impaction, mortality were analyzed.
**Results:** Demographic data, indication for ERCP, comorbidity, anticoagulation agent, and ASA class were similar in each group. There was no significant difference between the two groups in dose of sedative agent, dose of analgesics, and procedure time. The rate of pancreatic duct cannulation and acquisition of pancreatogram in the left lateral group were significantly higher than those in the prone group (9/30, 30.0% vs. 3/31, 9.7%, P = .046; 7/30, 23.3% vs. 1/31, 3.2%, P = .020). However, there was no significant difference in the rate of post-ERCP pancreatitis between the two groups (6/30, 20% vs. 5/31, 16.1%, P = .694). The rate of technical success and adverse event were similar between the two groups (96.8% and 40% in left lateral, and 100% and 32.3% in prone, respectively). There was no severe adverse event in each group.
**Conclusion:** The efficacy and safey of ERCP in the left lateral position was not inferior to those in the prone position.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0196 QUALITY OF ERCP IN A DISTRICT GENERAL HOSPITAL IN UNITED KINGDOM

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**Introduction:** Endoscopic Retrograde Chlangiopancreatography (ERCP) is a procedure that combines endoscopy and fluoroscopy to visualize the bile and pancreatic ducts. ERCP can be used to diagnose, as well as treat, various conditions. Common conditions treated include gallstones, inflammatory strictures, bile leaks, and cancer. ERCP is generally considered to be a safe procedure, however like any procedure there will always be associated complications such as pancreatitis, bleeding, perforation, infections, and sedation risk. Of the aforementioned complications pancreatitis is the most frequent; occurring in about 3 to 5 percent of people undergoing ERCP.
**Aims & Methods:** The aim of the audit is to evaluate and compare our clinical practice against the recommendations and standards set by the Joint Advisory

Group on Gastrointestinal Endoscopy (JAG) and with British Society of Gastroenterology (BSG) audit of ERCP. We did a retrospective review of all ERCP performed during 12 months period between April 2015 to April 2016. The data was collected from Unisoft Endoscopy database and the Electronic Discharge Note (EdN).

**Results:** Two Gastroenterologists and one Surgeon carried out a total of 209 procedures on 177 patients during the study period. Of which 157 (75.11%) were routine procedures. The mean age was 66.92 years (range: 18–95 yrs.). 112 (63.27%) were females and 43 (24.29%) were patients over 80 years. Indication of ERCP were as follows: Choledocholithiasis/Cholelithiasis- 145 (69.37%), biliary and pancreatic ductal abnormalities (leak, strictures)- 14 (6.69%), stent removal- 8 (3.82%), stent replacement- 4 (1.91%), ampullary/papillary abnormalities (Sphincter of Oddi dysfunction)- 3 (1.43%), no indication listed- 35 (16.74%). Deep CBD cannulation with intended intervention completion was 179 (85.64%); partially/unsuccessful cannulation was 20 (9.56%). Sphincterotomy was carried out in 30 (14.35%) and stone removal in 33 (15.78%). Procedure related complication was 5 (2.39%)- of which pancreatitis 3 (3.26%) and minor bleed 2 (0.95%). 2 (0.95%) patients were given Midazolam >5 with no subsequent complication. Patient performance state (ASA) was recorded in 57 (27.27%), of which 21 (10.04%) had ASA score of 3 or more.

**Conclusion:** In this study group the primary duct cannulation rate was above the national average and to expected JAG standards. Complication rates and procedure-related, well within expected national average and JAG standards. Less than third of patients had their ASA status recorded; this requires more attention in future, as it is essential in order to determine the appropriateness of the procedure.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0197 ENDOSCOPIC PAPILLARY LARGE BALLOON DILATATION (EPLBD) FOR EXTRACTION OF COMMON BILE DUCT STONES


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**Introduction:** Endoscopic papillary large balloon dilatation (EPLBD) is increasingly accepted as an appropriate option in management of difficult common bile duct (CBD) stones. Given the minor incision necessary, the short procedure time, the reduced requirement for mechanical lithotripsy (ML) and the low frequency of adverse events, EPLBD may be applied in patients who cannot tolerate wide endoscopic biliary sphincterotomy (EBS).

**Aims & Methods:** The aim of our work was to evaluate the safety and efficacy of EPLBD with a relatively large balloon (15–20 mm) in extraction of difficult CBD stones. 40 patients with calcular obstructive jaundice and dilated CBD (≥10 mm) subsequent to a single large stone (≥10 mm) or multiple stones (≥3) were recruited. All patients were subjected to endoscopic retrograde Cholangio-Pancreatography (ERCP) with limited sphincterotomy and large balloon dilatation followed by stone extraction using extraction balloon or dormia basket without lithotripsy, stenting or further ERCP sessions.

**Results:** Successful stone extraction was achieved in 34 patients (85%), while failure of stone extraction occurred in 6 patients (15%). The noted complications were minimal pancreatitis in 4 cases (10%), mild pancreatitis in 2 cases (5%), cholangitis in 2 cases (5%) and bleeding in 2 cases (5%), while no recorded cases of perforation or mortality subsequent to our procedure.

**Conclusion:** EPLBD is a safe and efficient procedure for extraction of difficult CBD stones and may be advisable in patients with high bleeding risk or abnormal papillary anatomy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0198 COST-EFFECTIVENESS OF CYANOACRYLATE GLUE INJECTIONS VERSUS ENDOSCOPIC ULTRASOUND GUIDED TREATMENT IN THE MANAGEMENT OF GASTRIC VARICES


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**Introduction:** Bleeding from gastric varices (GV) is severe and the mortality associated is high. Treatment with cyanoacrylate (CYA) glue injection has demonstrated higher hemostasis (>90%) and lower rebleeding rates compared to band ligation or sclerotherapy. However pulmonary embolism is one of its main adverse effects. It is a serious and sometimes fatal complication that is seen in 4.3% of the cases and depends on the volume of glue injected. Currently endoscopic treatments with CYA can be performed under direct visualization using a standard gastroscope or by Endoscopic Ultrasound (EUS) guidance with the injection of CYA alone or in combination with coils. Treatment under EUS guidance may improve results by precise targeting of the varix lumen and afferent feeding vein, allowing obliteration with less volume of CYA than the "blind" injection with standard endoscope. Coils are small metal devices with attached synthetic fibers that work retaining the CYA within varix lumen, reducing the volume needed for obliteration and risk of embolism. Variceal bleeding is the most costly of all digestive diseases in terms of hospitalization charges and there is little information in the literature on the economic impact of these treatments.

**Aims & Methods:** The aim of this study is to compare cost-effectiveness of GV treatment with two different techniques, CYA glue injections using a standard gastroscope vs. coils plus CYA guided by EUS. **Methods:** observational, descriptive and retrospective study with case collection from November 2014 to March 2016. Patients included had GV type GOV II or IGV I according to the to the Sarin classification. The indication of treatment was active bleeding, history of previous bleeding due to GV (secondary prophylaxis) or high-risk GV according to Baveno VI consensus (primary prophylaxis). Outcome measures included costs of the procedure, technical success, rebleed and complications rate.

**Results:** 36 patients (19 in CYA group and 17 in coils + CYA group) were included. The mean age was 61.45 (7–87) years old and 20 (55.5%) were men. 24 had GOV II GV and 12 IGV I. All patients enrolled in CYA group had active bleeding as the mean indication, unlike coils + CYA group that had active bleeding (41.2%), secondary prophylaxis (47.1%) and primary prophylaxis (11.8%) as indications. Mean varix size was 21.5 mm and mean number of procedures 1.23 (1.47 in CYA group and 1 in coils + CYA group). CYA group used more volume of glue than coils + CYA group (2.15 ml vs. 1.65 ml, p 0.018) and the mean number of coils was 2.1. There was a high technical success in both groups (CYA 84.2% vs. coils + CYA 100%) with a complication rate of 15.8% (2 pneumonia and 1 death) in CYA group; and 11.8% (1 episode of fever and 1 transient abdominal pain) in coils + CYA group (Table 1). Although mean total procedure cost was lower in CYA patients (US $1350.3 vs. US $ 2978) there was a significant difference in mean hospitalization cost (CYA = US $9710.6 vs. coils + CYA = US $70.46).

**Conclusion:** The overall cost showed that GV treatment with coils + CYA EUS-guided is more cost-effective than the use of CYA alone.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0199 FIDUCIAL MARKER PLACEMENT (FMP) FOR IMAGE-GUIDED RADIATION TREATMENT: EVALUATION OF THE IMPACT FOR RADIOTHERAPY IN OESOPHAGEAL AND RECTAL CANCER (FIDUCOR STUDY)


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**Introduction:** Radiation therapy (RT) has an important role in the treatment of oesophageal and rectal cancer. Delineation target of the lesion is often difficult during RT. Some series showed the potential use of fiducial markers (FM). FM has a supposed role to target the lesions, although there was no proved data in the literature.

**Aims & Methods:** Prospective registered study with inclusion from September 2014 to December 2015. Criteria for inclusion were oesophageal or rectal cancer with indication of RT, and lesions could be be crossed with EUS-scope (Slim US-scope, EG-3270UK). All patients underwent a simulation CT-scan before FMP and after FMP. All patients underwent gastroscopy, EUS, and CT-scan before the first simulation CT-scan. FM were placed under EUS and X-Ray guidance in a sedated patient. FM were gold markers of 5 mm length preloaded in a 22 G needle (Cookmedical®). FM were placed at the top and at the inferior part of the tumour. In case of visible lymph nodes, FM were placed after

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**Table 1:** Baseline data and results.

| | | CYA (n = 19) | Coils + CYA (n = 17) | Total (n = 36) | p value |
|---|---|---|---|---|---|
| Age, years (mean, range) | | 59.9 (7-87) | 63.3 (44-76) | 61.45 (7-87) | 0.146 |
| Sex (F/M), n | | 9 / 10 | 7/ 10 | 16/20 | 0.709 |
| Indication, n (%) | Acute bleeding | 19 (100%) | 7 (41.2%) | 26 (72.2%) | 0.001 |
| | Primary prophylaxis | 0 | 2 (11.8%) | 2 (5.5%) | |
| | Secondary prophylaxis | 0 | 8 (47.1%) | 8 (22.2%) | |
| Type of GV, n (%) | GOV II | 12 (63.1%) | 12 (70.5%) | 24 (66.6%) | <0.01 |
| | IGV I | 7 (36.9%) | 5 (29.5%) | 12 (33.3%) | |
| Mean varix size, mm (range) | | 20.4 (10-40) | 22.6 (12-32) | 21.5 (10-40) | 0.276 |
| Number of procedures, n | | 28 | 17 | 45 | |
| Mean number of procedures, n | | 1.47 | 1 | 1.23 | <0.01 |
| Mean volume of CYA, ml (range) | | 2.15 (0.6-2.4) | 1.65 (1.2-2.4) | 1.52 (0.6-2.4) | 0.018 |
| Mean number of coils, n (range) | | 0 | 2.1 (1-3) | 2.1 (1-3) | N/A |
| Technical success, n (%) | | 16/19 (84.2%) | 17/17 (100%) | 33/36 (91.6%) | 0.087 |
| Early rebleeding, n (%) | | 3/19 (15.8%) | 0 | 3/36 (8.3%) | 0.087 |
| Adverse events, n (%) | | 3/19 (15.8%) | 2/17 (11.8%) | 5/36 (13.8%) | 0.727 |
| Treatment modality, n (%) | Ambulatory | 6 (31.5%) | 16 (94.1%) | 22 (61.1%) | <0.01 |
| | Hospitalization | 13 (68.4%) | 1 (5.9%) | 14 (38.9%) | |
| Length of hospitalization, days (mean, range) | 3.36 (0–14) | 0.1 (0–1) | 1.8 (0–14) | <0.01 | |
| Area of hospitalization, days (mean, range) | Intensive Care Unit | 2.1 (0–11) | 0 | 1.1 (0–11) | <0.01 |
| | Intermediate Care Unit | 1.3 (0–14) | 0 | 0.7 (0–14) | 0.025 |
| | Emergency | 0 | 0.06 (0-1) | 0.03 (0–1) | 0.030 |
| Cost per procedure, US $ | | 816.7 | 2247 | | |
| Mean cost per procedure, US $ (± SD) | | 1203.5 ± 687 | 2247 | | <0.01 |
| Mean Coils cost (1 coil = US $ 300), US $ (±SD) | | 0 | 630 ± 197.5 | | <0.01 |
| Mean CYA cost (1 bleb x 0.3 ml = US $ 20.5), US $ (± SD) | | 146.7 ± 92.5 | 113.3 ± 20.7 | | 0.019 |
| Mean total procedure cost, US $ (± SD) | | 1350.3 ± 766.5 | 2978 ± 199.5 | | <0.01 |
| Mean hospitalization cost, US $ (range) | | 9710.6 (0–45857.2) | 70.46 (0–1197.8) | 5158.3 | <0.01 |
| **Mean total treatment cost (procedure + hospitalization),US $ (range)** | | **11060.9**(919.2–49575) | **3048.5**(2629–3867.8) | 7277.2 | <0.01 |

CYA: cyanoacrylate, F: female, M: male, GV: gastric varix, GOV: gastro-esophageal varices, IGV: isolated gastric varices; US $: United States Dollar

confirmation of metastic lymph nodes on pathological EUS-FNA reading. Evaluation criteria for usefulness of FMP in delineation target was the variation of growth tumor volume (GTV) and clinical target volume (CTV) before and after placement of FM. The GTV contours and the CTV contours were outlined in 3 dimensions. Modifications between both CT scan were considered as significant if axial (x) or coronal (y) variation was ≥5 mm or sagittal variation was ≥10 mm, or if target volume variation was ≥20%.
**Results:** 29 patients were included. All fiducial procedures could be achieved. 2 patients were excluded. One for unavailability of FM, one because of technical problem with the simulation CT-scan before FMP. A total of 15 oesophagus cancer and 12 rectal cancer were studied (13 and 10 men respectively). No complication were reported. FM migration occurred for one FM in one patient. The GTV changed significantly in 89% of the cases (13/15 for oesophagus cancer, 11/12 for rectal cancer), mainly due a difference in sagittal dimension with a mean of 21 mm and >10 mm for 67% (18/27) of the patients. The difference in sagittal dimension was >10 mm for 80% (12/15) of oesophagus tumours and for 50% (6/12) of the rectal tumours.
6 (1 oesophagus, 5 rectum) patients had a significant movement of the isocentre with a mean of 23 mm [6–40mm]. The oesophagus tumour was not seen with TDM in one patient. One (7%) patient had a distant lymph node metastasis in oesophagus cancer not seen with CT-scan.
GTV variation had also impact on global GTV and clinical tumor volume (CTV) in respectively 96% (15/15 oesophagus cancers and 11/12 rectal cancers) and 96% also (14/15 oesophagus cancers and 12/12 rectal cancers).
**Conclusion:** Placement of FM has an impact in target delineation in RT for oesophagus and rectal cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0200 HIGH YIELD OF CORE TISSUE FOR HISTOLOGICAL ANALYSIS WITH HIGH DIAGNOSTIC ACCURACY OF EUS-FINE NEEDLE BIOPSY USING THE 22 G AND 25 G SHARKCORE™ NEEDLES: A MULTICENTER RETROSPECTIVE STUDY

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**Introduction:** Procurement of tissue core biopsy samples may overcome some of the limitations of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). Novel designs of EUS-guided biopsy needles (EUS-FNB) may improve the procurement yield and the diagnostic capability.
**Aims & Methods:** We aimed to assess the safety, yield for a histological sample and diagnostic accuracy of the newly developed 25-gauge (25 G) and 22-gauge (22 G) SharkCore™ histology needles. The innovative needle tip geometry is designed with six cutting edge surfaces and an opposing bevel to acquire cohesive units of tissue with intact architecture and to minimize tissue fracturing. Data from consecutive patients with solid lesions who underwent EUS-fine needle biopsy (EUS-FNB) using the 25 G and 22 G SharkCore™ needles were retrospectively retrieved from the database of 4 tertiary care centers. A visible core was defined as an architecturally intact-looking piece of tissue deemed sufficient for histologic evaluation. Samples positive for malignancy were considered diagnostic. For patients with negative EUS-FNB, surgical specimen evaluation, results of other diagnostic investigations and/or long-term clinical follow-up (6 months) were used to establish the definitive diagnosis.
**Results:** During the study period, 147 patients underwent EUS-FNB using the SharkCore™ needles. Definitive diagnosis was available for 141 (96%) of them (M/F: 73/68; mean age 64 ± 12 years). Ten patients underwent sampling of two sites for a total of 151 solid lesions biopsied. There were 110 (72.8%) pancreatic lesions, 11 (7.3%) hepatic/bile duct lesions, 14 (9.3%) submucosal tumors, and 16 (10.6%) other lesions biopsied, with a mean diameter of 2.9 ± 1.1 cm (Table). In 80 cases the 22 G needle was used, while the 25 G needle was utilized in the remaining 71 cases. A mean of 3.5 ± 1.2 passes per lesion site was performed, without any major complications. A visible core was procured in 90.1% of cases, while in 6.0% a specimen for cytologic evaluation was obtained. In 80.1% of cases a definitive diagnosis of malignancy was made, while in 19.9% there was a benign condition. Considering malignant vs. non-malignant disease, the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy were 92.2% (95% CI, 86.1–95.8), 98.4% (95% CI, 86.3–99.8), 99.6% (95% CI, 95.9–100), 76.3% (95% CI, 61.1–86.8), 57.1 (95% CI, 3.65–844.18), 0.079 (95% CI, 0.043–0.146), and 94.0% (95% CI, 90.1–98.0), respectively. Regarding needle size, the visible core procurement yield and diagnostic accuracy (malignant vs. non-malignant disease) for the 25 G and 22 G needles were 83.1% vs. 96.3%, p < 0.001 and 90.1% vs. 97.5%, p = 0.08, respectively. 7 of the 9 non-diagnosed cases belonged to the 25 G subgroup, despite the fact that there was a tendency of performing more needle passes with the 25 G than with the 22 G needle (3.7 ± 0.2 vs. 3.4 ± 0.1, p = 0.06). The presence of a visible core was associated with a higher diagnostic accuracy for malignancy (97.1% vs. 66.7% in procedures where no

visible core has been obtained, $p < 0.01$). The core procurement yield was further influenced by the number of passes: for 3 or more passes, the core procurement yield was 95% vs. 75% for 2 or less passes ($p < 0.01$). However, this did not influence diagnostic accuracy.

| Lesion location | N | Median no. of passes (n, range) | Visible core present (%) | Diagnostic yield (%) (malignant vs. non-malignant disease) |
|---|---|---|---|---|
| **Pancreas** | 110 | 3.6 (1-7) | 90.1 | 94.6 |
| **Liver/bile ducts** | 11 | 2.5 (2-3) | 81.8 | 81.8 |
| **Submucosal tumors** | 14 | 3.9 (3-5) | 85.7 | 92.9 |
| **Other** | 16 | 3.1 (2-5) | 100 | 100 |

**Conclusion:** The 22 G and 25 G SharkCore™ needles are able to gather tissue for EUS-FNTA of solid lesions with very good procurement and diagnostic yields after a minimum number of passes. The 22 G-size needle showed superior core procurement and diagnostic capabilities. However, large prospective studies on their performances are warranted to further evaluate the use of these novel types of needles.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0201 UTILITY OF CONTRAST-ENHANCED ULTRASONOGRAPHY FOR DIFFERENTIAL DIAGNOSIS OF BILIARY TRUCT DISEASE

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**Introduction:** Although contrast-enhanced ultrasonography (CE-EUS) provides high spatial resolution and enable precise blood flow imaging, few study have reported its use for biliary tract disease.
**Aims & Methods:** The aim of this study is to investigate the value of CE-EUS for differential diagnosis of biliary tract disease. The present study enrolled 53 consecutive patients with confirmed biliary tract disease who underwent CE-EUS in Yokohama City University Medical Center between April 2009 and December 2015. The cohort included 36 men and 17 women, with a mean age of 61.4 years. EUS examinations were performed using UE260 and UCT260 (Olympus Medical Systems, Tokyo, Japan). Ultrasound image analyses were performed using Prosound $\alpha$10 (Hitachi Aloka Medical Systems, Tokyo, Japan). When B-mode US detected biliary tract disease, a bolus infusion of contrast agent (15 μL/kg Sonazoid (Daiichi Sankyo, Tokyo, Japan)) was administered, and contrast harmonic images were obtained for 90 s. All clips were stored on a hard disk, and blinded investigators evaluated the intensity, heterogeneity, and persistence of contrast effect retrospectively. Then, the sensitivity, specificity, and accuracy for diagnosis of malignant lesions were determined on the basis of characteristic findings.
**Results:** Final diagnoses were based on histological findings, and benign status was confirmed by follow-up for at least 1 year. Nineteen patients were found to have benign lesions (7 patients had sclerosing cholangitis and 12 had conditions), and 33 had malignant lesions (25 had extra-hepatic cholangiocarcinoma, 3 had gallbladder cancer, and 4 had other cancers). CE-EUS could detect enhancement in all lesions. After contrast infusion, 17 cases (89%) of benign lesions and 27 cases (81%) of malignancies showed hyper-enhancement in the arterial phase. Fifteen cases (79%) of benign lesions showed persistent enhancement in the venous phase, while 13 cases (61%) of malignancies showed a decrease in enhancement ($p < 0.05$). In the 39 cases in which strictures were found on B-mode EUS (12 benign lesions and 27 malignant lesions), luminal narrowing was seen on CE-EUS in 9 cases (75%) of benign lesions and but no cases of malignancy. The sensitivity, specificity, and accuracy of CE-EUS for differentiating benign lesions from malignancies using these findings were 94%, 73%, and 85%, respectively.
**Conclusion:** CE-EUS was useful to differentiate benign and malignant case of biliary tract disease in the present study. We believe this modality has clinical benefits, especially, for lesions for which are difficult to reach the pathological confirmation of diagnosis is difficult.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0202 ETOMIDATE VERSUS PROPOFOL ADMINISTRATION DURING ENDOSCOPIC ULTRASONOGRAPHIC PROCEDURES: A PROSPECTIVE DOUBLE-BLINDED RANDOMIZED CONTROLLED TRIAL

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**Introduction:** Although a growing body of evidence demonstrates that propofol-induced deep sedation can be effective and performed safely, cardiopulmonary adverse events have been frequently observed. Etomidate is a new emerging drug that provides hemodynamic and respiratory stability, even in high-risk patient groups.
**Aims & Methods:** The objective of this study was to compare safety and efficacy profiles of etomidate and propofol for endoscopic sedation. A total of 128 patients undergoing endoscopic ultrasound were randomized to receive either etomidate or propofol blinded administered by a registered nurse. Endpoints comprised cardiopulmonary adverse events, efficacy, patient satisfaction, and sedation profiles.
**Results:** The incidence of oxygen desaturation (4/64 [6.25%] vs. 20/64 [31.25%], $P = 0.001$) and respiratory depression (5/64 [7.81%] vs. 21/64 [32.81%], $P = 0.001$) was significantly lower in the etomidate group than in the propofol group. All cardiovascular episodes were self-limited, controlled completely without special intervention, and lacked significant difference between both groups. The frequency of myoclonus was significantly higher in the etomidate group (22/64 [34.37%]) compared with the propofol group (8/64 [12.50%]) ($P = 0.012$). Repeated measure analysis of variance revealed significant effects of sedation group and time on systolic blood pressure (etomidate group > propofol group). Physician satisfaction was greater in the etomidate group than in the propofol group.
**Conclusion:** Etomidate administration resulted in fewer respiratory depression events and had a better sedative efficacy than propofol; however, it was more frequently associated with myoclonus and increased blood pressure during endoscopic procedures.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0203 ENDOSCOPIC ULTRASOUND-GUIDED INJECTION OF GEMCITABINE-LOADED IRON OXIDE NANOPARTICLES IN THE PORTAL VEIN AS A THERAPEUTIC OPTION FOR PANCREATIC CANCER METASTASES

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**Introduction:** The poor prognosis of pancreatic cancer (PAC) has developed a continuous need for new potential therapies. Because most of the times PAC is diagnosed in highly advanced stages, when hepatic metastases have occurred, chemotherapy remains the main option for cancer patients. Gemcitabine is currently used for many cancer types including PAC, however the maximum tolerated dose in humans is restricted by its side effects on healthy cells.
**Aims & Methods:** Our objective was to assess a new developed gemcitabine-loaded iron oxide nanoparticles (IONs) after portal vein injection in an experimental pig model. Six domestic pigs were used for our study design, of which three were injected under endoscopic ultrasound guidance with gemcitabine-IONs in the portal vein and other three in the jugular vein. All endoscopic equipment was intended for animal use only, while the procedures were performed according to the national and international guidelines for animal use in research. After identifying the portal vein, 2 ml of gemcitabine-IONs were injected using a 19 gauge EUS-FNA needle, with live monitoring on EUS-imaging. A day after the procedure, necropsy was performed and liver, heart, spleen, kidneys and pancreas were harvested and sent to pathologic examinations, mass spectroscopy and x-ray diffraction assessment.
**Results:** No technical difficulties were encountered, with a mean time per procedure of 5.23 minutes. The portal vein was easily identified, with no major complications or additional bleeding. Pathologic examinations with multispectral imaging assessment showed large ION deposits in all macrophages-like organs, especially in the liver ($6526.35 \pm 290.62 \mu m^2$) after portal vein injection. Liver iron concentrations were significantly higher after portal vein injection than systemic procedures. Hepatic concentrations of gemcitabine were significantly higher after portal vein injection than systemic injection.
**Conclusion:** Gemcitabine – ION levels after portal vein injection were significantly higher in the liver which indicated that the gemcitabine was still loaded on the nanoparticles and may result in a prolonged drug exposure. EUS-guided injection of gemcitabine loaded iron oxide nanoparticles may offer better outcomes on therapeutic options for hepatic metastases for PAC.
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**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0204 THE HIGH DIAGNOSTIC PERFORMANCE OF EUS-ASSISTED SINGLE- INCISION NEEDLE-KNIFE (SINK) BIOPSY MAY AVOID FURTHER ENDOSCOPIC FOLLOW-UP OF SMALL UPPER SUBEPITHELIAL TUMORS

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**Introduction:** The optimal management strategy for small subepithelial tumors (s-SETs) is unknown. Current guidelines recommend EUS to characterize upper SETs and annual follow-up for those smaller lesions (≤2 cm). However, this approach is not evidence-based and is associated to a very poor compliance (< 50%, Kushnir et al, *GIE* 2015). EUS-guided SINK biopsy may provide and all-at-once definitive diagnosis able to save from iterative endoscopic procedures. The study is aimed at assessing the histologic/diagnostic performance and outcomes of EUS-SINK biopsy for upper s-SETs as a single procedure.

**Aims & Methods:** This is a retrospective chart review of a prospectively-mantained database from April'10 to Oct'15 including all consecutive patients with small (≤2 cm) foregut SETs referred for EUS study. They all underwent radial EUS study and then, linear EUS exploration for size/layer/morphological characterization and doppler to discard presence of vessels. Then a needle-knife sphincterotome was used in endocut mode at 30–60 W settings to perform a 6 mm linear incision over the highest convexity area of the target lesion. Finally, a conventional biopsy forceps was deeply introduced through the hole to retrieve 3 to 5 samples. Patients were discharged one hour thereafter and contacted by telephone one and seven days later to discard complications.

**Results:** 93 patients with SETs were referred (M/F: 50/43; mean age: 60.23, range 20–89) Small SETs: 42/93 (45.16%): mean diameter s-SETs: 1.19 cm (0.65–2). Organ location: Esophagus (5) Stomach (31) Duodenum (6). Echolayer: 2nd /3rd /4th: 5/24/13. Only 3 samples were non-diagnostic or included just mucosal tissue: Yield of SINK biopsies: 39/42: 92.85%. Histologic diagnoses- table 1-: Lipoma (2), leiomyoma (3), GIST (15), Abrikosoff's tumor (1), heterotopic pancreas (13), gangliocytic paraganglioma (1), Inflammatory fibroid polyp (5), duplication cyst (1), neuroendocrine tumor (1). IH analysis (CD117-CD34) was feasible in 13/15 GISTs (86.66%). There were no procedural-related complications.

**Conclusion:** SINK biopsy provides an all-in-one time, effective and safe method for accurate diagnosis of small upper SETs. This one-step technique may avoid conventional endoscopic follow-up which is hampered by costs and low compliance with standard surveillance recommendations.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0205 CLINICAL IMPACT OF EUS TREATMENT OF WOPN WITH DEDICATED DEVICES: A RETROSPECTIVE ANALYSIS

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**Introduction:** Infected Walled-Off Pancreatic Necrosis (WOPN) is the main life-threatening complication of acute pancreatitis. Superiority of trans-gastric endoscopic necrosectomy over surgical necrosectomy was demonstrated[i]. However, standard endoscopic techniques were associated with long procedural time, stent migration and bleeding, pointing out the need of dedicated devices. Recently, a dedicated lumen apposing metal stent (LAMS) was designed to create an anastomosis between the WOPN cavity and the gut lumen in a single-step procedure.

**Aims & Methods:** The primary aim of this study was to evaluate the survival rate and clinical efficacy of EUS-guided drainage of infected WOPN with LAMS and subsequent Direct Endoscopic Necrosectomy (DEN). Survival was evaluated at 1 and 3 months after the first procedure. Clinical success was evaluated as recovery from sepsis and other WOPN-related symptoms associated with disappearance of WOPN at CT scan after LAMS removal without the need for additional endoscopic or surgical intervention. Secondary outcomes were to evaluate technical success, adverse events, procedure time, number of endoscopic procedures, and duration of hospital stay. All consecutive patients with infected WOPN who underwent LAMS placement and DEN between February 2014 and February 2016 were retrospectively reviewed. This novel device was directly advanced under EUS guidance into the cavity by using the electrocautery tip. After deployment of the LAMS, the echoendoscope was removed, and a standard gastroscope was inserted to perform immediate DEN.

**Results:** A total of 19 patients (mean age 59.8 years, female 31.5%,) underwent DEN. LAMS placement and necrosectomy (technical success) was achieved in 18 (94.9%) patients. Mean procedure time was 42.9 minutes. Mean number of sessions was 3.9 (1–9). Three patients underwent double LAMS placement, through the stomach and duodenum. Clinical success was achieved in 15/18 (83.3%) patients. Mean length of hospital stay was 19 days (3–43). Median follow up was 261 days (IQR 270). No adverse events occurred. A total of 3 patients died during the study period: the survival rate was 84.2% and 78.9% at 1 and 3 months after procedure.

**Conclusion:** This study on EUS treatment of patients with infected WOPN with dedicated LAMS demonstrates excellent efficacy and safety of the procedure with significant impact on survival in this setting of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0206 CONCORDANCE BETWEEN MAGNETIC RESONANCE CHOLANGIO-PANCREATOGRAPHY (MRCP) AND ENDOSCOPIC ULTRASOUND FOR THE EVALUATION OF MORPHOLOGICAL FEATURES OF CYSTIC PANCREATIC TUMORS

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**Introduction:** Morphological evaluation of cystic pancreatic tumours (CPT) for the detection of worrisome features and high-risk stigmata is required for the correct management of these lesions. Magnetic resonance cholangio-pancreatography (MRCP) and endoscopic ultrasound (EUS) are considered the techniques of choice for the morphological evaluation and follow-up of CPT.

**Aims & Methods:** Aim of the study was to evaluate the concordance between these two techniques in this setting. Methods: Retrospective analysis of a prospectively collected database of CPT. Patients undergoing both EUS and MRCP for the study of CPT were included over a period of 5 years. Time between EUS and MRCP should be shorter than 6 months for final inclusion. EUS was performed by linear Pentax echoendoscopes (EG-3870UTK y EG-3270UK) and HITACHI-ASCENDUS and PREIRUS ultrasound equipment. MRCP was performed by SIEMENS equipment. Location, number and size of PCT, and presence of worrisome features and high-risk stigmata according to Fukuoka criteria were evaluated. Concordance between EUS and MRCP was evaluated by Kappa score.

**Results:** 97 patients fulfilled inclusion criteria (mean age 66 years, range 25–87, 64 females). Number and size of lesions were similarly evaluated by EUS and MRCP. Individual worrisome features and high-risk stigmata were present in up to 12% of patients. A poor agreement between EUS and MRCP ($k < 0.2$) was found for wall thickness, non-enhanced mural nodules, enhanced solid component, and dilatation of the main pancreatic duct (MPD) > 10 mms. Agreement was fair ($k = 0.21–0.40$) for MPD dilatation of 5–9 mms, and moderate ($k = 0.41–0.60$) for the location of the CPT and abrupt change of the MPD. There was no agreement between the two techniques in the evaluation of lymph nodes.

**Conclusion:** EUS and MRCP provide similar information about number, size and location of CPT, but the concordance between the two techniques is poor to fair for the detection of the majority of worrisome features and high-risk stigmata. These findings deserve confirmation in larger studies including a higher number of lesions with worrisome features and high-risk stigmata.

**Disclosure of Interest:** J.E. Domínguez-Muñoz: International Advisor Pentax. All other authors have declared no conflicts of interest.

## P0207 FACTORS INFLUENCING THE ACCURACY OF EUS-GUIDED TISSUE ACQUISITION FOR THE EVALUATION OF ENLARGED LYMPH NODES

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**Introduction:** Endoscopic ultrasound (EUS)-guided tissue acquisition is an accurate technique for the evaluation of both mediastinal and intra-abdominal enlarged lymph nodes.

**Aims & Methods:** Aim of our study was to evaluate factors associated with the diagnostic yield of EUS-guided tissue acquisition in this setting.

Methods: Retrospective analysis of a prospectively collected database of patients who underwent a EUS-guided tissue acquisition for the pathological diagnosis of enlarged lymph nodes over the last 3 years. EUS were performed under conscious sedation with Pentax linear echoendoscopes (EG-3870UTK and EG-3270UK) and the HITACHI ultrasound device. Tissue acquisition was performed with both cytological and histological EUS needles of different sizes. Samples were

processed in a cytological solution (cytolit). The impact of lymph node location and size, number of passes and type of needle used on the accuracy of EUS-guided tissue acquisition was evaluated. Final diagnosis was based on surgical histopathology or, in non-operated cases, on EUS-guided tissue acquisition, imaging assessment (CT scan and/or PET scan), with a minimum clinical follow-up of 6 months. Data are shown as percentage, median and range, and were analyzed by logistic regression. Diagnostic accuracy was also evaluated.
**Results:** 175 lymph nodes on 159 patients were sampled in the study period, with a median size of 20 mm (range 12.5–27 mm). 94 lymph nodes (53.7%) were located at mediastinum and 81 (46.3%) were intra-abdominal. Histology needles (ProcoreTM) were used in 107 (61.1%) cases, and cytology needles in the remaining 68 lymph nodes (38.9%). Final diagnosis was benign/reactive origin in 88 cases (50.3%), carcinoma in 70 cases (40%), and lymphoma in 17 (9.7%). Sensitivity, specificity, positive predictive value and negative predictive value of EUS-guided tissue acquisition for the detection of malignancy was 75.9%, 100%, 100% and 80.7%, respectively. Overall accuracy was 87.9% (95%IC 72.1–87.7). None of the factors evaluated influenced the diagnostic accuracy of EUS-guided tissue acquisition.
**Conclusion:** EUS-guided tissue acquisition is a very accurate technique for the differential diagnosis of enlarged lymph nodes. Diagnostic accuracy of this technique is not influenced by the location or size of the lymph nodes evaluated, the number of needle passes nor the type of needle used.
**Disclosure of Interest:** J.E. Domínguez-Muñoz: International advisor Pentax.
All other authors have declared no conflicts of interest.

## P0208 PREP-LESS COLON CANCER SCREENING USING A NOVEL X-RAY IMAGING CAPSULE

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**Introduction:** Bowel preparation is likely the most significant reason for low participation in screening colonoscopy, while poor preparation impairs adenoma detection. A CRC screening method that would generate structural data of thecolon, without cathartic cleansing or diet restrictions, would offer an attractive alternative for many patients from the target population that are not willing to undergo colonoscopy. In preliminary studies: Colon reconstructions from synthetic phantoms, bovine cadaver and live swine showed spatial resolution of 2–3 mm in colon diameter measurements, and detection of implanted polyps >= 6 mm.
**Aims & Methods: Device:** The capsule is similar in dimensions to other approved capsules. The capsule emits ultra-low dose X-rays, which are scattered by ingested contrast agent mixed with colon contents, and sensed by detectors in the capsule to generate high-resolution 3-dimensional (3D) imagery of the colon without bowel cleansing. The capsule is activated and scans the inner surface only when the capsule is propelled within the colon. **Aim:** To evaluate the safety and correlation between the capsule and colonoscopy findings **Methods and Patients:** The system performed scans upon detecting of effective capsule motion in the colon and transmitted imaging data to an external recorder unit attached to patients' lower back. Combined data from colon scans and the CPS system were used to reconstruct 3D colon segments in nonprepped colons. Total transit time and total Xray exposure were calculated to assess the safety profile of the capsules. Between 1.3.13 -9.2.16 scanning capsules were swallowed by 52 subjects, and tracked throughout the alimentary tract using an external capsule positioning system (CPS). The capsule was activated to scan only while moving in the colon, and transmitted imaging data to the CPS to reconstruct 3D colon segments. Total transit times were measured. X-ray exposure was calculated to assess safety in human subjects.
**Results:** Seventy five dummy capsules passed naturally and uneventfully confirming the safety of the capsule. Scanning capsules were swallowed uneventfully in all 52 patients, and naturally and eliminated in 51/52 patients, after 64.3 ± 36.4 hours. One capsule was extracted via colonoscopy during a planned polypectomy. The volunteers were exposed to an ultralow total radiation dose of 0.03 ± 0.0007 mSv (equivalent to 1 chest X-ray) for the entire procedure. The capsule detected polyps of different size, shape and location in the colon. Capsule routes and 3D reconstructions of colon lumen and outer surface were obtained from all participants. Both pedunculated and sessile polyps were clearly seen and validated by colonoscopy. There were no reports of capsule malfunction or damage which might have compromised the participants' safety. Fifty capsules (out of 52 that were ingested) were returned to the lab. They were all in perfect shape.
**Conclusion:** A novel X-ray imaging capsule for colorectal cancer screening appears safe and capable of prep-less colon imaging in an human study. Quantitative ultra-low dose X-ray imaging and detection of polyps of different sizes and polyp types was achieved in the colon of human subjects. Efficacy validation of this X-ray-based CRC screening technology is being conducted in a multi-center prospective study.
**Disclosure of Interest:** N. Arber: CONSULTATION FEE: BIO-VIEW, CHECK-CAP, BAYER STOCK SHAREHOLDER: MICROMEDIC, GI-VIEW.
All other authors have declared no conflicts of interest.

## P0209 CAPSULE ENDOSCOPY SCORES FOR ASSESSMENT OF INFLAMATORY ACTIVITY OF SMALL-BOWEL IN CROHN'S DISEASE

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**Introduction:** Capsule endoscopy (CE) represents the non-invasive method with the highest sensitivity in the evaluation of small-bowel mucosa in Crohn's disease (CD).[1] Recent recommendations advocate the employment of validated CE scores for the assessment of small-bowel inflammatory activity in CD, allowing a standardized description of lesions and an objective assessment of severity and follow-up.[1, 2] Lewis Score (LS) and Capsule Endoscopy Crohn's Disease Activity Index (CECDAI) are the two validated scores currently available, but comparative studies are scarce.[3, 4] Moreover, evidence concerning the correlation of these endoscopic scores with biomarkers and clinical activity in small-bowel CD is lacking.
**Aims & Methods:** The primary aim of this study was to compare LS with CECDAI and to determine cutoff values for CECDAI similar to those of LS (135 and 790). The second aim was to correlate LS and CECDAI with biomarkers and symptoms. All patients with CD who underwent CE between March 2010 and February 2016 were included. LS and CECDAI were determined after analysis of each CE. In patients with CD confined to the small-bowel, C-reactive protein (CRP) and Harvey-Bradshaw index (HBI) were evaluated. Statistical analysis: Spearman's correlation coefficient and linear regression analysis. Significance: $p < 0.05$.
**Results:** Fifty-three patients were included, 60.4% (n = 32) were women, with a mean age of 41.8 years. CD was restricted to the small-bowel in 64.2% (n = 34) of patients and in the remaining 35.8% (n = 19) the activity was ileocolonic. Mean values obtained for LS were 1147 (+/-1453), CECDAI 11.3 (+/-6.9), CRP 0.92 (+/-1.5) mg/dL and HBI 2.4 (+/-2.8). There was a very strong correlation between LS and CECDAI ($r_s = 0.878$; $p < 0.0001$). In linear regression analysis, thresholds values of 135–790 in LS corresponded to 7.7–10.3 cutoff values in CECDAI, respectively, with an accuracy of 62.3%. Neither CRP correlated with LS ($r_s = 0.068$; $p = 0.72$) or CECDAI ($r_s = -0.004$; $p = 0.98$), nor HBI with LS ($r_s = -0.15$; $p = 0.40$) or CECDAI ($r_s = -0.10$; $p = 0.23$).
**Conclusion:** Correlation between the two CE activity scores was very strong, with LS thresholds of 135 and 790 corresponding to CECDAI values of 7.7 and 10.3. HBI and CRP had no correlation with endoscopic activity scores in small-bowel CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0210 THE SENSITIVITY OF THE PILLCAM SB3 VIDEO CAPSULE IN COMPARISON TO THE PILLCAM SB2 REGARDING THE DETECTION OF THE PAPILLA VATERI

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**Introduction:** Recently the PillCamSB3 capsule endoscopy system was introduced. In comparison to the PillCamSB2 the new capsule has a wider angle of view, an increased resolution and an adaptive frame rate from 2 to 6 frames per second depending on the speed of capsule movement. The aim of this study was to investigate if these developments lead to an increased sensitivity of the new capsule system. As the duodenal papilla is a finding that is present in everyone but only visualized in 10.4% with older capsule systems [1] it appears to be an ideal target lesion for the investigation of the diagnostic accuracy of a new capsule system.
**Aims & Methods:** The capsule endoscopy procedures between 01/2011 and 04/2015 with the PillCamSB2 and SB3 were reviewed. Exclusion criteria included endoscopic introduction of the capsule, polyposis syndromes, overt bleeding/poor visibility/gaps in the duodenum and previous surgery with alteration of the gastric and/or duodenal anatomy. The review was done by one experienced

reader frame by frame during the passage of the entire duodenum. The detection rate of the papilla and the number of frames in which the papilla was visualized were compared.
**Results:** 181 capsule procedures were included in this study, 84 with the PillcamSB3 and 97 with the Pillcam SB2 system. There were no differences in the detection rate of the papilla (11/84 vs. 12/97, p = 0.884) and the number of frames that showed the papilla (11.91 vs. 14.00, p = 0.155 (-21, 208–17, 026)).
**Conclusion:** The sensitivity of the PillCamSB3 system is not superior to the SB2 system regarding the detection of the papilla vateri.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0211 CLINICAL USEFULNESS OF CLASSIFICATION BY CAPSULE ENDOSCOPY FOR DETECTION OF RADIATION ENTERITIS

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**Introduction:** Radiation enteritis is a radiation-induced injury of the gastrointestinal (GI) tract and a major complication of radiotherapy. Capsule endoscopy (CE) may be a useful diagnostic tool for radiation enteritis of the small intestine, which standard endoscopy cannot evaluate. However, there are few reports regarding detection of radiation enteritis by CE.
**Aims & Methods:** We aimed to assess the Clinical usefulness of classification by CE for detection of radiation enteritis. We selected patients with the possibility of radiation enteritis who had previously treated with radiotherapy on the abdomen or pelvis. To increase diagnostic the yield of radiation enteritis, CE was performed in patients having anemia or chronic abdominal pain. We used PillCam® SB and SB2 (Given Imaging Ltd.) for the CE. Lesions were described according to the Capsule Endoscopy Structured Terminology (CEST). Pathological findings were classified into three groups (modified Saurin's classification), according to their relevance to radiation enteritis. P0:no relevance, P1:potential relevance, P2:high relevance.
**Results:** Fifteen consecutive patients were enrolled between May 2011 and January 2016. The median age was 66 years (54–79). The median radiation dose was 55 Gy with range of 3671.12 Gy. In one case, bowel patency was not confirmed by patency capsule evaluation. CE diagnosed radiation enteritis occurs in 12 of 14 patients (P2: 50%, P1: 36%). Congested mucosa and Yellow villi were the most frequent abnormal lesions. Although no patient experienced capsule retention, one drawback was that the CE impacted at the stenosis. In the follow-up period ranging from 109 to 1732 days (median 1344 days), ileus occurred in 3 cases among 7 cases that have been diagnosed as P2. Correspondence between ileus and P2 classification was significantly high.
**Conclusion:** CE was shown to be useful for detecting radiation enteritis. We recommend performing CE first when radiation enteritis is suspected.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0212 SMALL INTESTINE CAPSULE ENDOSCOPY FOR THE EVALUATION OF OBSCURE GASTROINTESTINAL BLEEDING IN THE ELDERLY

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**Introduction:** Obscure gastrointestinal bleeding (OGIB) in the elderly is often caused by angioectasia and/or mucosal injury. We examined elderly patients (≥65 years) with OGIB, according to the World Health Organization criteria and our report (*Gastrointest Endosc* 2015;81:AB479). Cases of OGIB significantly increased with intake of oral antithrombotic agents among the elderly due to prolonged small intestine transit time. These findings also suggest the involvement of chemical mucosal disorders. In this study, we classified patients according to 10-year increments to clarify the effects of age on the occurrence of OGIB.
**Aims & Methods:** We used small intestine capsule endoscopy (CE) to examine 506 patients in this hospital between April 2004 and March 2016. We classified the patients according to age (group A, <55 years; group B, ≥55 to ≤65 years; group C, ≥65 to ≤75 years; group D, >75 years) and compared the symptoms, oral medication use, and small intestine transit times between the groups.
**Results:** A total of 506 patients were enrolled in the study, with 169, 96, 131, and 110 patients in groups A, B, C, and D, respectively. Antithrombotic drugs were administered in 4.7% (8), 15.6% (15), 20.6% (27), and 27.3% (30) of patients in groups A, B, C, and D, respectively. The use of antithrombotic drugs significantly increased with age ($P < 0.01$). Angioectasia and/or mucosal injury were demonstrated in 25% (2), 20.0% (3), 44.4% (12), and 46.7% (14) of patients in groups A, B, C, and D, respectively. Small intestine transit times were 254.5, 283.4, 301.6, and 313.5 min in groups A, B, C, and D, respectively. Although the small intestine transit time was significantly shorter in group A compared to groups C and D ($P < 0.01$ and $P < 0.01$, respectively), no significant differences were observed among the other three groups.
**Conclusion:** The use of oral antithrombotic drugs increased with age, along with the concomitant findings of angioectasia and/or mucosal injury. The small intestine transit time was significantly longer in elderly people who were at least 65 years. These findings suggest the development of OGIB in the elderly. Therefore, in cases of OGIB in the elderly, we should consider utilizing CE in monitoring for mucosal disorders related to intake of antithrombotic drugs, particularly in patients older than 65 years.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0213 VALIDATION OF THE COMPUTED ASSESSMENT OF CLEANSING SCORE IN MIROCAM® CAPSULE ENDOSCOPY SYSTEM

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**Introduction:** Capsule endoscopy (CE) represents a safe diagnostic procedure in small-bowel mucosal assessment.[1] The presence of debris and air bubbles negatively impairs the diagnostic yield of CE and the evaluation of the quality of small-bowel cleansing is necessary to assess the reliability of findings.[2] A computed assessment of cleansing (CAC) score was developed to objectively evaluate small-bowel cleansing in the PillCam® CE system and to overcome the subjectivity and complexity of previous scoring systems.[1]
**Objectives:** Adapt the CAC score to the Mirocam® system, evaluate its reliability with the Mirocam® CE system and compare it with three validated subjective grading scales.
**Methods:** Thirty CE were prospectively and independently reviewed by 2 authors (RP, AP) who classified the degree of cleanliness of the small-bowel according to a quantitative index (QI), a qualitative evaluation (QE) and an overall adequacy assessment (OAA).[2] The authors were blinded for the CAC score of each CE, which consisted of ([mean intensity of the red channel]/[mean intensity of the green channel]–1) x10. The mean intensities of the red and green channels of the small-bowel segment of the "Map View" bar of Miroview Client® were determined using the histogram option of a photo-editing software. Statistical analysis: Spearman's correlation coefficient, intraclass correlation coefficient (ICC), unweighted kappa and student's t-test. Significance: $p < 0.05$.
**Results** The mean grade for the QI was 7.47 (+/-1.74) for reader-1 and 7.9 (+/-1.67) for reader-2, resulting in an excellent inter-reader reliability with an ICC of 0.92 (CI95% = 0.84–0.96). The classification in excellent/good/fair/poor of the QE was obtained in 13.3%/53.3%/26.7%/6.7% CE for reader-1 and in 20%/46.7%/23.3%/10% for reader-2, with an excellent concordance between both readers with an ICC of 0.83 (CI95% = 0.68–0.91). The degree of cleanliness in OAA was considered adequate in 86.7% of cases by reader-1 and 90% of cases by reader-2, with an unweighted kappa of 0.84. A good correlation between the QI and the computed scores was found with a $r_s = 0.5$ ($p = 0.005$) for reader-1; $r_s = 0.48$ ($p = 0.008$) for reader-2; and $r_s = 0.49$ ($p = 0.006$) for the mean of both readers. A fair correlation between QE and the computed scores was found with an ICC of 0.43 (CI95% = 0.089–0.68, $p = 0.008$) for reader-1 and 0.45 (CI95% = 0.11–0.70, $p = 0.006$) for reader-2. The mean values of CAC for adequate/inadequate levels of cleanliness for OAA were 5.16/3.45 ($p = 0.02$) for reader-1 and 5.07/3.66 for reader-2 ($p = 0.09$).
**Conclusion:** There was a strong agreement between both CE readers for each of the three subjective scales used. The CAC score is feasible in the Mirocam® CE system and correlates with the validated subjective scales.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0214 CAPSULE ENDOSCOPY WITH PILLCAM SB2 VERSUS PILLCAM SB3: DID TECHNOLOGICAL IMPROVEMENT GRANT A STEP FORWARD IN CLINICAL PRACTICE?

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**Introduction:** Small bowel capsule endoscopy (SBCE) is a diagnostic tool with increasing relevance. Pillcam® SB3 has better image resolution than PillCam® SB2 and adaptive frame rate technology, rendering it potentially more effective. **Aims & Methods:** Compare findings detection and completion rate between PillCam® SB2 and SB3. **Methods:** Retrospective single-center study including 357 consecutive SBCE, 173 SB2 and 184 SB3. Videos were reviewed and findings were recorded and classified as relevant or not.
**Results:** Patients had a mean age of 48 years with 66.9% females. The two main indications were suspicion/staging of inflammatory bowel disease (IBD) and obscure gastrointestinal bleeding (OGIB), (43.7% and 40.3%, respectively). Median small-bowel (SB) transit time was 261 minutes (IQR ± 122) and overall completion rate was 95% (339/357). Endoscopic findings were reported in 76.2% of the examinations, while relevant findings corresponded to 53.5%. The most frequently reported findings were SB ulcers, in 29.4% of patients. Findings in gastrointestinal segments other than the SB were reported in 20.4% of SBCE, most frequently in the stomach (16.8%). No significant differences were found when comparing SB2 with SB3 regarding completion rate (93.6% vs 96.2%, $p = 0.27$), overall endoscopic findings (73.4% vs 78.8%, $p = 0.23$), relevant findings (54.3% vs 52.7%, $p = 0.76$), first tercile findings (43.9% vs 48.9%, $p = 0.35$), extra-SB findings (23.7% vs 17.3%, $p = 0.14$), after-8 hours findings (8.1% vs 8.2%, $p = 0.99$), Z line and papilla detection rate (35.9% vs 35.7%, $p = 0.97$ and 27.1% vs 32.6%, $p = 0.32$, respectively). Regarding the subgroup of patients with suspicion/staging of IBD, a significant difference was found in the detection of villous edema and 3rd tercile findings, favoring SB3 (26% vs 44%, $p = 0.02$ and 47% vs 66%, $p < 0.02$, respectively). No differences were found on Lewis score classification and 3rd tercile ulcer detection. In patients with OGIB, mucosal atrophy was significantly more frequently diagnosed with the PillCam ® SB3 (0% vs 8%, $p = 0.03$).
**Conclusion:** Overall, PillCam ® SB3 didn't improve diagnostic yield nor the completion rate compared with SB2. Nevertheless, when particular indications were analyzed, significant differences in detection of villi alteration, such as atrophy and segmental villous edema, were found, which may eventually be attributable to SB3 better image resolution.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0215 WHOLE-LIVER CT TEXTURE ANALYSIS TO PREDICT THE DEVELOPMENT OF METACHRONOUS COLORECTAL LIVER METASTASES – A MULTICENTRE STUDY

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**Introduction:** Texture analysis refers to a mathematical approach to quantify heterogeneity on imaging. Commonly used measures are 'entropy' (a measure of heterogeneity) and 'uniformity' (a measure of homogeneity). Previous research showed promise for texture analysis of the liver on CT in patients with colorectal cancer to assess whether or not metastases are present within the liver.[1, 2] Apparently diffuse changes in liver texture occur due to the presence of metastatatic liver disease, which are probably related to diffuse changes in liver perfusion or the presence of microscopic disease throughout the liver. The hypothesis is that such changes may already be present and detectable by texture analysis before any metastases become visible on CT and that CT-texture analysis may thus predict which patients are at risk to develop metachronous liver metastases. **Aims & Methods:** Aim of this multicenter study was to test this hypothesis and assess whether CT-texture can predict the development of metachronous metastases before they become visible on CT. To investigate this 165 patients (from 3 centres) were included and divided into three subgroups: patients [A] without metastases for >2 years after primary diagnosis (n = 57), [B] with synchronous metastases (n = 54) and [C] who developed metachronous metastases within 24 months after primary diagnosis (n = 54). Whole-liver texture analysis was performed on primary staging portal-phase CT by manual delineation of the apparently non-diseased liver parenchyma. The texture parameters mean grey-level intensity (M), entropy (E) and uniformity (U) were derived with different image filter values (unfiltered = 0.0, fine = 0.5, medium = 1.5, coarse = 2.5). Image filtration was applied to highlight structures of different size within a tissue. Univariable logistic regression analysis was performed (group A vs. B) to identify potentially predictive texture and clinical parameters (e.g. age, sex, primary tumour site, T- and N-stage and CEA). The best predictors were subsequently tested in multivariable analyses to differentiate between group A and C (i.e. predict metachronous disease). Receiver Operator Characteristics (ROC) curve analysis was performed to test the diagnostic performance of the different clinical and texture variables to predict metachronous metastases. Subgroup analyses were performed for patients with early (≤6 months), intermediate (7–12 months) and late (13–24 months) metastases.
**Results:** Univariable analysis identified $U_{0.5}$ and the clinical parameters sex, primary tumour site, N-stage and CEA as potential predictors. For the early metastases subgroup, $U_{0.5}$ remained a significant predictor in multivariable analysis (OR 0.56, $p = 0.05$), resulting in an AUC of 0.74 to predict metachronous disease within 6 months. Adding $U_{0.5}$ to the clinical parameters CEA + N-stage resulted in an AUC of 0.78 to predict early metastases, which was a tendency towards significant improvement compared to only N-stage + CEA ($P = 0.08$). None of the texture or clinical parameters were able to predict metachronous metastases within 12 or 24 months.
**Conclusion:** Whole-liver CT texture analysis may have additional value to more well-known clinical parameters such as N-stage and CEA to predict upfront which patients are at risk to develop metastases within six months after primary diagnosis. It is, however, not robust enough to predict patients at risk to develop metastases within 24 months.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0216 DEFINITION OF AGE-DEPENDENT REFERENCE VALUES FOR DIAMETER OF THE COMMON BILE DUCT AND PANCREATIC DUCT ON MRCP FROM A POPULATION-BASED COHORT STUDY

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**Introduction:** Changes in diameters of the pancreaticobiliary ducts are markers of diseases including benign conditions like chronic pancreatitis, bile duct stones or pancreaticobiliary malignancies. MRCP (magnetic resonance cholangiopancreatography) is the first line, non-invasive imaging modality for duct configuration, with broad availability and ever increasing accuracy. However, the reference ranges in asymptomatic individuals and their change with age and after medical procedures have only been studied in small cohorts.
**Aims & Methods:** To define new reference values for diameters of pancreaticobiliary ducts on MRCP in the general population and to identify factors influencing duct size. Study subjects were recruited from the general population-based SHIP and had whole body MRI + MRCP (1.5 T MRI system). Diameters of pancreatic duct (PD) and common bile duct (CBD) were measured on MRCP maximal intensity projection sequence before and after administration of secretin by an investigator blinded to other subject data.
**Results:** 1385 subjects were initially scanned, 865 measured PDs and 938 CBDs were included for further analysis. Subjects were excluded for missing data or evidence of pancreaticobiliary disease (post-cholecystectomy n = 115, cholecystolithiasis n = 57, choledocholithiasis n = 8, chronical pancreatitis n = 17, pseudocysts n = 52, cholestasis n = 11, liver cirrhosis n = 1, hepatitis n = 2). Median age was 53 y (21–89 y) and 48.5% were female. The diameters increased with age (PD median (range) 1.-3. Quartile: 20–29 years 1.33 cm (1.20–1.57), >70 years 2.49 (1.85–3.01); CBD median (range) 1.-3. Quartile: 20–29 years 4.53 (3.87–5.17), >70 years 6.50 (5.10–8.23)) and the historic upper limit of normal of 3 mm for PD and 7 mm for CBD were exceeded by 11% and 18.2% respectively. Subjects that underwent cholecystectomy presented with significantly increased diameter of CBD, but not PD ($CBD_{w/oCCE}$: 5.30 mm ± 1.893 SD vs. $CBD_{w/CCE}$: 8.18 mm ± 2.841 SD, $p < 0.01$; $PD_{w/oCCE}$: 1.84 mm ± .778 SD vs. $PD_{w/CCE}$: 2.06 mm ± .868 SD, $p > 0.01$). Duct size was not correlated to liver function tests (ASAT, ALAT, γGT). Using quantile regression on the 95th percentile age and gender dependent upper limits for normal duct size were defined (<70 years PD male 3.77 cm, female 3.76 cm; CBD male 9.16 cm, female 10.70 cm; >70 years PD male 4.12 cm, female 4.35 cm; CBD male 10.32 cm, female 12.44 cm). PD but not CBD diameters significantly changed after administration of secretin. Upper limits of normal PD size after secretin were (<70 years $PD_{sec}$ male 4.33 cm, female 4.11 cm; >70 years $PD_{sec}$ male 5.95 cm, female 4.74 cm).
**Conclusion:** Up to 18% of healthy volunteers would have undergone diagnostic workup for enlarged CBD or PD above the current reference standard. The width of the pancreaticobiliary ducts increases in an age dependent manner in asymptomatic volunteers. An increase of the CBD after cholecystectomy can be observed, whereas the PD remains unaffected. In cases of no signs of cholastatic liver disease a moderately increased duct diameter is most likely non pathologic.

So to reduce healthcare expenditure and unnecessary workup age and gender-related adjustments of the reference values are suggested to avoid unnecessary diagnostic workup.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0217 A PILOT STUDY OF PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FOR GASTROINTESTINAL NEOPLASMS: AN INITIAL EXPERIENCE IN JAPAN

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**Introduction:** Probe-based confocal laser endomicroscopy (pCLE) allows real-time, in vivo high-resolution imaging of the gastrointestinal epithelium at a cellular level. There are only a few publications on pCLE in the additional diagnostic value of gastric and colorectal neoplasms. We conducted a pilot study to investigate the diagnostic yield of pCLE in the evaluation of neoplastic and non-neoplastic gastric lesions and non-invasive and invasive colorectal neoplasms. (UMIN000016557).
**Aims & Methods:** This study was conducted by two referral centers. A total of 38 patients were referred for the treatment of gastric or colorectal lesions between February and May 2015. All participating clinicians had web-based self-training of pCLE. High-definition white light endoscopy (WLE), chromoendoscopy (CE), and magnified narrow band imaging (M-NBI) were performed on all lesions. pCLE was then performed to differentiate between non-neoplastic or neoplastic gastric lesions and non-invasive or invasive colorectal neoplasms based on Miami classification (on-site diagnosis). All neoplastic lesions were treated by endoscopy or surgery. An off-line review was performed on all lesions by a separate expert endoscopist who was blinded to the clinical information. All the still images of WLE, CE, and M-NBI and the video of pCLE were reviewed. The clinician independently scored the gastric lesions as neoplastic or non-neoplastic and the colorectal lesions as adenoma/slight invasion (M-SM) or deep invasion (SM) for each endoscopic imaging modality. We then evaluated the sensitivity, specificity, accuracy of each endoscopic imaging modality and inter-observer agreement of pCLE. The histology was the gold standard.
**Results:** 17 patients had a total of 24 gastric lesions and 21 patients had 22 colorectal lesions. 14 gastric lesions were neoplastic (median tumor size: 12.5 mm (2–38), histology: differentiated-type/undifferentiated-type adenocarcinoma = 11/3, depth of invasion: mucosa/slight submucosa/deep submucosa (≥500 μm) = 10/1/3). 10 were non-neoplastic. Sensitivity/specificity/accuracy (%) of pCLE in on-site diagnosis was 79/90/83. The sensitivity/specificity/accuracy (%) for the off-line review were as follows; WLE = 50/90/67, CE = 57/70/63, M-NBI = 64/80/71, and pCLE = 79/70/75. The inter-observer agreement of pCLE between on-site diagnosis and off-line review, kappa value was 0.67 (95%C.I.:0.37–0.96). 22 colorectal lesions were characterized as follows; (adenoma/M-SM slight/SM deep: 7/10/5). The sensitivity/specificity/accuracy (%) for the on-line diagnosis were as follows; WLE = 83/100/96, M-NBI = 100/100/100, CE = 100/100/100. Either of lack of structure or thickened epithelium in pCLE findings was seen in 80% of SM deep invasion (4/5) and 12% of adenoma/M-SM slight invasion (2/17). Sensitivity/ specificity (%) was 80/88. When these pCLE findings applied for depth diagnosis in off-line review, the sensitivity/specificity/accuracy (%) of pCLE in off-line review were 60/88/82, respectively. The inter-observer agreement of pCLE between on-site diagnosis and off-line review, kappa value was 0.58 (95%C.I.:0.14–1.02).
**Conclusion:** pCLE may be useful in the differentiation between neoplastic and non-neoplastic gastric lesions and depth diagnosis for colorectal lesions. Further study should be conducted to validate these findings.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0218 THE DIAGNOSTIC PERFORMANCE OF CT IN DETECTING COLORECTAL PERITONEAL METASTASES

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**Introduction:** Cytoreductive surgery (CRS) is the treatment of choice for peritoneal carcinomatosis (PC). In order to achieve a significant survival gain a complete cytoreduction is essential in the surgical treatment of PC of colorectal carcinoma. In case of peritoneal PC and colon carcinoma cytoreduction is combined with hyperthermic intraperitoneal chemotherapy (HIPEC). Whether a complete cytoreduction is feasible is determined by the amount and localization of disease in the abdomen. In colorectal cancer the Dutch region count is a scoring system using surgical inspection to assess the amount and localization of disease. Currently a diagnostic laparoscopy is often used to inspect all areas in the abdomen and to predict whether a complete cytoreduction is feasible. However, with this invasive procedure it is not always feasible to inspect all relevant areas in the abdomen due to the presence of adhesions and / or tumor. It would therefore be more than helpful if a radiological diagnostic tool could accurately assess the amount and localization of peritoneal disease before any surgery in order to predict the possibility of achieving a complete cytoreduction. A better selection of the group of patients in whom a complete cytoreduction is feasible will limit the number of ineffective and expensive procedures.
**Aims & Methods:** This study aims to compare the extent of PC on computed tomography (CT) with the peroperative findings of PC and long-term survival. Preoperatieve abdominal CT scans of patients who underwent CRS-HIPEC, performed between January 2005 and September 2015, were evaluated by two experienced radiologists. The extent of PC according to the Dutch region count was scored, in which the abdominal cavity is divided into seven regions. When five or less abdominal regions were affected CRS-HIPEC was considered useful and thus executed. Peroperative region count was the reference standard. Diagnostic performance of CT was calculated and survival analyses were performed.
**Results:** Two hundred thirty-four patients were included. The accuracy for selecting PC patients with a good or bad prognosis with CT was 87%, based on a region count of five or less. Forty-nine scans were evaluated by two radiologist and inter-observer variability for a continuous region count was calculated (k = 0.139). Patients with five or less affected abdominal regions on CT imaging showed significant lower disease free survival (median 20.5 months; IQR 18.0–23.0) and overall survival (median 39.5 months; IQR 32.5–46.5) compared to patients with more affected abdominal regions (median 2.8 months; IQR 0.0–7.6 and median 9.3 months; IQR 0.0–21.7) ($p < 0.001$ and $p = 0.002$).
**Conclusion:** These results show that CT can select patients who could benefit from CRS-HIPEC. Survival rates significantly decreased when more abdominal regions on CT were affected.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0219 DIAGNOSTIC VALUE OF IMAGING FOR THE DETECTION OF PERITONEAL METASTASES: A META-ANALYSIS

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**Introduction:** Peritoneal seeding is a well-known mechanism of spread in advanced gastrointestinal cancer. Peritoneal carcinomatosis (PC) has significant implications for not only treatment options but also prognosis; it is the second-most frequent cause of death in colorectal cancer patients after metastatic disease to the liver. The last few decades showed a revolution in the treatment of PC. Presently the prognosis of PC patients has dramatically improved and where once only palliative treatments and comfort measures were contemplated, nowadays selected patients benefit from a radical locoregional approach aiming at long-term disease control. That radical locoregional approach consists of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). When a complete surgical cytoreduction can be achieved 5-years survival rates of up to 50% are reported after CRS-HIPEC. Therefore, it is important to detect patients with peritoneal metasasis.
**Aims & Methods:** To determine the diagnostic value of imaging in detecting peritoneal carcinomatosis in staging cancer patients. A literature search of Ovid, Embase and Pubmed was performed to identify studies reporting on the accuracy of imaging for the detection of PC for colorectal, gastric and gynaecological cancers. Data extraction was performed by two observers in consensus. The sensitivity, specificity, and diagnostic odds ratio (DOR) were calculated using a bivariate random effects model and hierarchical summary operating curves (HSROC) were generated.
**Results:** The search resulted in 4165 articles. 35 relevant studies fulfilled all the required inclusion criteria of >15 patients and surgery/histology/clinical follow-up as reference standard. From these 35 articles 42 datasets could be extracted for analysis; 21 for CT, 5 for MRI, 5 for PET and 11 for CTPET.

**Table 1:** Results meta-analysis.

| | Pooled Sensitivity | Pooled Specificity | DOR |
|---|---|---|---|
| CT | 73% (CI:60-83%) | 90% (CI:84-94%) | 25.6 (CI:13.3-49.1) |
| MRI | 78% (CI:69-85%) | 88% (CI: 83-92%) | 26.6 (CI: 14.7-48.4) |
| PET | 53% (CI: 32-75%) | 98% (CI: 94-99%) | 55.7 (CI:19.4-159.9) |
| CTPET | 87% (CI:74-94%) | 87% (CI:69-95%) | 46.0 (CI: 16.2-130.4) |

**Conclusion:** This meta-analysis shows that CTPET seems to be the most optimal imaging modality for the detection of PC. CT and MRI demonstrate similar results in detecting PC with a lower pooled sensitivity than CTPET.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0220 MR IMAGING FOR DEDICATED LOCAL STAGING OF COLON CANCER

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**Introduction:** Distant and local staging of colon cancer is currently performed with computed tomography (CT). At diagnosis, 15–23% of colorectal cancer (CRC) patients have liver metastasis detection is crucial because it entails poor prognosis and a different clinical approach and treatment. Multiple studies already demonstrated that magnetic resonance imaging (MRI) is superior to CT for the detection of liver metastasis[1]. It seems local staging of colon cancer does not need the same finesse; imaging is mostly used to assess the resectability of the colon tumor (i.e. involvement of surrounding organs). However, this might change in the near future; a large multicenter study, FOXTROT[13], is currently investigating the benefits of neo-adjuvant chemotherapy for patients with locally advanced colon cancer. If the FOXTROT trial confirms initial promising reports, neoadjuvant treatment in colon cancer patients will be adopted as standard therapy, just like in rectal cancer patients. If so, preoperative imaging will become a crucial tool to select patients for neo-adjuvant treatment. MRI is well established in local staging of rectal cancer because of its superior results compared to CT[14]. However, little is known about the local staging of colon cancer with MRI. If MRI is able to accurately stage colon tumors, it might be the ideal imaging tool for simultaneous local and distant staging.
**Aims & Methods:** The aim of this study was to evaluate the diagnostic performance of MRI for local staging of colon cancer patients. 55 colon cancer patients underwent MRI (1.5 T; T2TSE and DWI) of the abdomen and were retrospectively analysed by two blinded, independent readers. Histopathology after resection was the reference standard. Both readers evaluated tumour characteristics being; invasion through bowel wall (T3/T4 tumours), invasion beyond bowel wall of $\geq$5 mm and/or invasion of surrounding organs (T3cd/T4), serosal involvement, extramural vascular invasion (EMVI) and the presence of malignant lymph nodes (N+). Inter-observer agreement was compared using Kappa ($\kappa$) statistics.
**Results:** The sensitivity and specificity detecting T3/T4 tumours (35/55), T3cd/T4 tumours (15/55), fascia involvement (8/55), EMVI (17/55) and nodal involvement (19/55) were for reader 1; 91%/84%, 40%/88%, 88%/74%, 100%/62% and 47%/86%, 68%/64% and for reader 2: 72%/89%, 60%/75% and 75%/72% 88%/70%, respectively. Interobserver agreement between both readers were good to moderate: 0.72, 0.55, 0.62, 0.60 and 0.60 respectively.
**Conclusion:** Compared to previous literature on CT our study shows that MRI seems to perform as well as CT in local staging, with the added benefit that it has the potential to be more accurate in detecting prognostic factors such as serosal involvement and EMVI. This could have an important therapeutic impact, especially if neo-adjuvant treatment will be adopted in the treatment guidelines for advanced colon cancer (i.e. if the results of the FOXTROT trial confirm its benefit). An additional important advantage of MRI is its superiority in detecting small liver metastases with the evaluation of the colon tumor in one imaging session[1]. The most recent EURECCA expert guidelines advise MRI of the liver[2] in the preoperative staging of colorectal cancer. This would entail that the MR sequences for local staging of the colon tumor can be performed in the same MR imaging session of the liver. This combined approach could result in the most optimal abdominal staging tool for colon cancer patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0221 THE ROLE OF ENDOSCOPY IN PATIENTS WITH GASTROINTESTINAL WALL THICKENING DETECTED DURING ROUTINE IMAGING

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**Introduction:** Gastrointestinal wall thickening (GWT) is a common incidental finding in abdominal computed tomography (CT). Despite uncertain clinical significance, this finding often leads to expensive evaluation, especially in the fear of cancer.
**Aims & Methods:** We assessed the utility of endoscopic investigation in patients with GWT diagnosed by CT. We retrospectively evaluated patients performing upper gastrointestinal endoscopy (UGE) and colonoscopy (CP) following a diagnosis of GWT. Age, gender, previous oncologic history and endoscopic and pathology findings were recorded.
**Results:** We included 353 patients (53.8% female, mean age 66.2 $\pm$ 15.2 years) with GWT in the stomach (183) and colon (170). 161 patients (45.6%) had a normal endoscopic examination (51.4% UGE versus 39.4% CP). 142 patients (40.2%) presented only with benign lesions (39.3% UGE versus 41.2% CP). In 49 patients (13.9%) a high grade adenoma or cancer was diagnosed (8.7% UGE versus 19.4% CP). Only age was identified as an independent risk factor for the diagnosis of malignancy (OR 1.028, 95%CI 1.005–1.052, $p = 0.015$). A cancer was more likely to be found in CP than UGE (OR 2.60 95%CI 1.37–4.94, $p = 0.004$). Even though 61 patients (17.3%) had a prior history of cancer, this was not found to be predictive of a current diagnosis of carcinoma.
**Conclusion:** In our series, over 50% of patients presented with abnormal findings during endoscopic investigation of GWT and in 13.6% a diagnosis of cancer was performed. Our results support the investigation of GWT, especially in older patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0222 TRANSPARENTIZATION TECHNOLOGY ENABLES US TO RECONSTRUCT THREE-DIMENSIONAL HISTOPATHOLOGICAL STRUCTURE OF GASTROINTESTINAL MUCOSA NON-DESTRUCTIVELY: A PORCINE MODEL STUDY

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**Introduction:** There is no established method to assess three-dimensional structure of endoscopic resected gastrointestinal mucosa non-destructively.
**Aims & Methods:** This study was aimed to evaluate the feasibility of transparentization technology for three-dimensional histopathological assessment of resected gastrointestinal mucosa in a porcine model. Esophagus, stomach, and colon mucosa obtained from a sacrificed pig were prepared in the following two fashions; formalin-fixed specimen, and deparaffinized specimen after formalin-fixed paraffin-embedding. After staining with 4', 6-diamidino-2-phenylindole (DAPI) and lycopersicon esculentum lectinconjugated with DyLight 594 (tomato lectin), all specmens were transparentized by LUCID method (ilLUmination of Cleared organs to IDentify target molecules)[1] and observed by confocal laser scanning microscope (CLSM) and multiphoton-excited fluorescence microscope (MEFM). Scanned horizontal section views were evaluated after reconstruction of three-dimensional structures using image-analyzing software. After observation, all transparentized specimens were paraffin-embedded again. They were evaluated by conventional histopathological assessment including immunohistopathological staining to measure the impact of transparentization comparing to formalin-fixed paraffin-embedded specimen without transparentization.
**Results:** Degrees of transparency were increased well in all specimens, especially in deparaffinized specimens after formalin-fixed paraffin-embedding. CLSM and MEFM revealed horizontal section views of mucosa at deeper levels. MEFM enabled us to observe the whole thickness of mucosal layer and reconstruct three-dimensional structure. DAPI and tomato lectin staining revealed ductal structure and vessel structure, respectively. Paraffin-embedded specimens after transparentization were all assessed appropriately by conventional histopathological staining.
**Conclusion:** Transparentization technology enables us to observe deeper inside of endoscopic resected specimen and evaluate three-dimensional structure non-destructively.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0223 THE EVOLUTION OF THE ENDOSCOPE ASSISTED PERCUTANEOUS TRANS-ESOPHAGEAL GASTRO-TUBING AS A NEW ALTERNATIVE TO THE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: 86 SUCCESSFUL CASES

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**Introduction:** In 1994, percutaneous transesophageal gastrotubing (PTEG) was reported as an alternative procedure for feeding tube placement in patients for whom percutaneous endoscopic gastrostomy (PEG) is contraindicated. In 1997, the PTEG balloon was replaced with a rupture-free balloon (RFB) because the original balloon was easily punctured and could not support the esophageal lumen for guidewire insertion. In Japan, PTEG is commonly used for enteral nutrition and gastrointestinal decompression, and the standard PTEG procedure is performed under ultrasonographic and fluoroscopic guidance.
**Aims & Methods:** For safety, we began, in 2003, to perform endoscope-assisted PTEG (EA-PTEG), which has since been revised and assessed. The original RFB was used for the first 6 of 107 EA-PTEG procedures. Contact between the endoscope and the RFB was inadequate, so an endoscope-mounting RFB (EM-RFB) was devised for the tip of the endoscope. EA-PTEG was performed with the EM-RFB in 2 patients, but the balloon prevented smooth operation of the endoscope. In fact, in 1 of the 2 patients, EA-PTEG with the original RFB was necessary. The next new RFB was an overtube (OT-RFB) to allow for smooth endoscope operation. EA-PTEG with the OT-RFB was performed in 5 patients, but the OT-RFB obscured the ultrasonographic view needed for puncture. To resolve this problem, a double-layered RFB was fitted around the overtube, to which a window was added. Fluid was injected so that the outer RFB dilated the esophageal lumen and the inner RFB does so inward so that a clear ultrasonographic view could be obtained. This new RFB is referred to as the double-balloons equipped overtube type RFB (DBOt-RFB).
**Results:** The DBOt-RFB was used successfully in 86 patients—63 for enteral nutrition and 23 for gastrointestinal decompression. We had some difficulty at first: we were unable to obtain a safe puncture route in 3 patients, the endoscope caused vagus nerve hypotension in 1 patient, and hypoxia occurred in 1 patient. We resorted to using the original RFB in 1 of these patients and to standard PTEG in the other 4. We made several improvements to the DBOt-RFB, and the EA-PTEG procedure was performed with no major complications.
**Conclusion:** Because real-time assessment of the esophageal lumen is achieved endoscopically, the EA-PTEG procedure is not only safer than standard PTEG but also easier to monitor. The endoscopic view warns us of bleeding and/or mucosal injury and alerts us to contraindications. Should the endoscopic procedure prove ill-advised, we can convert to standard PTEG. EA-PTEG with DBOt-RFB is a safe, simple, minimally invasive cervical esophagostomy procedure.
**Disclosure of Interest:** H. OISHI: Patent royalties from Sumitomo Bakelite Co. Ltd.

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## P0224 TRANS-RADIAL ACCESS FOR ENDOVASCULAR ABDOMINAL INTERVENTIONS: A SAFE AND FEASIBLE TECHNIQUE

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**Introduction:** The number of endovascular abdominal interventions has increased over the past decades and is expected to increase even further in the near future. Examples of endovascular interventions in gastroenterology are trans-arterial chemoembolization (TACE) for hepatocellular carcinoma, mesenteric artery stent placement for occlusive chronic gastro-intestinal ischemia and embolization of hepatic artery aneurysm, hepatic adenoma or bleeding hepatocellular carcinoma. The approach for endovascular abdominal interventions is mostly trans-brachial or trans-femoral. Previous reports about trans-brachial and trans-femoral procedures for endovascular abdominal interventions report relatively high complication rates. Moons et al.[1] reported in 43 patients (trans-brachial $n = 32$) a minor complication rate of 25.6% (8 local hematoma, 1 dissection, 2 pseudo-aneurysms) and a major complication rate of 20.9% (1 pneumonia, 2 strokes, 1 spleen-infarction, 2 thrombosis, 1 AV-fistula, 2 nerve damages). In interventional cardiology nowadays, trans-radial access (TRA) is the preferred approach with low reported complication rates. Advantages of TRA compared to trans-brachial and trans-femoral access are reduced radiation exposure to the interventionalist and no requirement of ultrasound for the arterial puncture. Furthermore, no major anatomical structures with risk of damaging are nearby and collateral circulation exists via the ulnar artery. Finally, the closure device is inexpensive compared to femoral closure devices such as Angio-Seal and patients are permitted to mobilize immediately. TRA however requires longer catheters, especially in abdominal procedures, which can lead to difficulties in manipulation. Reports on endovascular abdominal interventions per TRA are lacking.
**Aims & Methods:** The aim of this study was to assess the feasibility and complication rate of TRA for endovascular abdominal interventions. We prospectively assessed the complication rates of patients who underwent endovascular abdominal intervention per TRA instead of trans-brachial or trans-femoral access between November 2014 and April 2016. All patients had a normal modified Allen test result, a simple test to assess the adequacy of blood supply through the ulnar artery to the hand.
**Results:** Forty-five patients (24 men, mean age $63.8 \pm 12.1$ years) underwent 49 trans-radial endovascular abdominal procedures. Thirty-one (63.3%) interventions concerned a mesenteric endovascular procedure, 11 (22.4%) TACE and 7 (14.3%) an endovascular procedure of the hepatic artery. The minor complication rate was 16.3% (6 local hematoma, 1 cellulitis, 1 temporary sensibility loss). There were no major complications. In 7 procedures successful execution was not achieved, in 3 out of 7 procedures possibly attributed to the radial approach. Therefore, radial technical success rate was 94%. All patients were able to mobilize directly after the intervention.
**Conclusion:** TRA for endovascular abdominal interventions showed to be a feasible and successful technique with a low complication rate. TRA may therefore be the preferred approach in endovascular abdominal interventions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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MONDAY, OCTOBER 17, 2016 10:30–17:00
**SURGERY I – POSTER EXHIBITION**

## P0225 IMPROVEMENT IN GLUCOSE METABOLISM AFTER BARIATRIC SURGERY: COMPARISON OF LAPAROSCOPIC ROUX-EN-Y GASTRIC BYPASS AND DUODENOJEJUNAL BYPASS LINER

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**Introduction:** Both Roux-en-Y gastric bypass (RYGB) and duodenojejunal bypass liner (DJBL) have been shown to induce significant weight loss and dramatically ameliorate type 2 diabetes mellitus (T2DM). Because DJBL implantation induces nutrient bypass of the duodenum, its mechanisms have been proposed to mimic those of the RYGB.
**Aims & Methods:** This monocentric prospective parallel group study aimed to compare the bariatric procedures DJBL and PYGB in the treatment of obesity and T2DM. Up to April 2016, a total of 54 patients were included. Twenty-five (8 male, mean age $51.1 \pm 10.9$ yrs) underwent RYGB and twenty-eight had DJBL (12 male, mean age $54.1 \pm 10.6$ yrs). Body weight, body mass index, and glycated haemoglobin A1C (HbA1C) were documented pre- and 1, 3, and 9 months postsurgery.
**Results:** Changes in metabolic parameters are shown in table 1.
**Conclusion:** This is the first study comparing the improvement in glucose metabolism following RYGB or DJBL. As expected, our preliminary data demonstrated RYGB to be superior for induction of weight loss. However, both procedures have a similar impact on diabetes remission, indicating that alteration of weight loss itself is not the main determinant of improvement in glucose homeostasis in these obesity procedures.
**Disclosure of Interest:** J. Stein: Jürgen Stein has received fees for lecturing and consultancy from GI Dynamics.
All other authors have declared no conflicts of interest.

**Abstract No: P0225**

| | RYGB | | | | | DJBL | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | pre | 1 mon | 3 mon | 9 mon | Δ* | pre | 1 mon | 3 mon | 9 mon | Δ* |
| Weight (kg) | 129.3 ± 22.0 | 117.0 ± 23.6 | 107.7 ± 17.9 | 97.6 ± 17.0 | 31.7 | 122.3 ± 28.8 | 120.4 ± 26.7 | 106.1 ± 15.1 | 108.0 ± 12.6 | 22.9 |
| BMI (kg/m$^2$) | 44.5 ± 6.4 | 39.1 ± 3.4 | 37.0 ± 5.6 | 34.1 ± 6.1 | 10.4 | 41.2 ± 8.3 | 40.4 ± 8.0 | 36.4 ± 5.2 | 36.3 ± 3.9 | 8.8 |
| $HBA_{1c\ (\%)}$ | 7.7 ± 1.1 | 7.2 ± 1.1 | 6.3 ± 1.2 | 6.2 ± 1.3 | 1.5 | 9.2 ± 1.9 | 8.5 ± 1.8 | 7.8 ± 1.4 | 7.6 ± 1.4 | 1.6 |

*compared to preintervention (pre).

## P0226 THE EFFECT OF SLEEVE GASTRECTOMY ON ESOPHAGEAL CHEMICAL CLEARANCE AND BASAL IMPEDANCE VALUES

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**Introduction:** Sleeve gastrectomy (SG) is one of the most performed procedure in the field of bariatric surgery. However, digestive symptoms such as gastroesophageal reflux disease (GERD), vomiting, regurgitations, food intolerance, or epigastric pain are also reported after this type of surgery. Currently, data are scarce on the exact impact of SG on esophagogastric physiology, in particular on the pathogenesis of ''de novo'' GERD.
**Aims & Methods:** We aimed to assess the impact of SG on esophageal chemical clearance and on basal impedance levels in morbidly obese without preoperative pathological GER by means of impedance-pH monitoring (MII-pH). We retrospectively reviewed data from a consecutive series of 18 women and 7 men (median age, 42 years) who underwent MII-pH before and after SG. All patients underwent a standardized questionnaire for symptom presence and severity, upper endoscopy, high resolution manometry (HRM) and MII-pH. By means of MII-pH, the following variables were assessed: distal esophageal acid exposure as percentage (AET%) of time with pH < 4 (abnormal if total time with pH < 4 was greater than 6.3%, and/or upright time with pH < 4 was greater than 4.2%, and/or recumbent time with pH < 4 was greater than 1.2%), number and quality (acid and weakly-acid) of reflux detected at MII (normal value < 73), and Symptom Association Probability (SAP). Esophageal chemical clearance was determined using the post-reflux swallow-induced peristaltic wave (PSPW). A PSPW was defined as an antegrade 50% drop in impedance relative to the pre-swallow baseline originating in the most proximal impedance site, reaching all the distal impedance sites, and followed by at least 50% return to the baseline in the distal impedance sites (bolus exit). For each impedance-pH tracing, the number of refluxes followed within 30 s by a PSPW was divided by the number of total refluxes (manual calculation) in order to obtain the PSPW index. The mean nocturnal esophageal basal impedance (MNBI) level was assessed from the most distal impedance channel during nighttime recumbent period. Three 10-minute time periods (around 1.00 am, 2.00 am, and 3.00 am) were selected and the mean baseline for each period was computed with the aid of the software. Time periods including swallows, refluxes and pH drops were avoided. The mean of the three measurements was manually calculated to obtain the MNBI. Parametric variables were summarized as mean and SD and compared using ANOVA. Nonparametric variables were summarized as median with interquartile range (IQR) and compared using Wilcoxon nonparametric tests (Kruskall–Wallis). A $p < 0.05$ was considered significant.
**Results:** The preoperative (130.8 kg (119–156), Body Mass Index (BMI) = 46.1 (38–58)) and postoperative (98 kg (72–110), BMI = 34.7 (28–46)) anthropology was statistically different with 56% excess weight loss. After surgery, the incidence of symptoms related to reflux was not modified; in particular, no increase in perception of heartburn, regurgitation, and epigastric pain was observed. The preoperative median percentage with esophageal pH < 4 was 1.47 for total time, 1.1 and 1 in the upright and recumbent positions, respectively. Postoperatively, DeMeester's score ($p = 0.041$) and the median percentage with esophageal pH < 4 in recumbent position ($p = 0.04$) significantly increased (from 1 (0–1.2) to 3.1 (0–4.2), $p = 0.04$). The SG produced an increase of total reflux episodes (33 vs. 53; $p < 0.0001$) detected at MII. Specifically, a significant increase of postoperative non-acid reflux episodes in both upright (17 vs. 28; $p < 0.0001$) and recumbent (4 vs. 8; $p < 0.0001$) position was detected. PSPW index decreased after SG (80 ± 10 vs. 50 ± 20; $p < 0.001$), as well as MNBI, that decreased (3016 ± 819 vs 1542 ± 452; $p < 0.001$). There was an inverse correlation between PSPW, MNBI and the number of reflux, and a inverse correlation between PSPW and AET ($p < 0.0001$).
**Conclusion:** SG can lead to an impairment of esophageal chemical clearance and mucosal integrity, as well as to an increase of reflux number. Due to this effect, SG should be considered only after an adequate preoperative esophageal testing to exclude an underlying GERD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0227 LONG TERM QUALITY OF LIFE AFTER ESOPHAGECTOMY WITH GASTRIC PULL-UP

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**Introduction:** Esophageal cancer (EC) is an increasingly common cancer with a poor prognosis. Health-related quality of life (HRQL) has become an important outcome measure of surgical treatment for cancer and recent systematic reviews showed a deterioration in HRQL after esophagectomy. Data about long-term adjustment to esophagectomy are scarce.
**Aims & Methods:** The aim of this study was to analyze long term quality of life at 3 or more years after esophagectomy for cancer. Patients who had undergone esophagectomy with gastric pull-up during 2007–2013 were interviewed regarding their alimentary satisfaction and quality of life. Quality of life was evaluated using the Italian version of the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and OG25. Data about patients characteristics, treatment and follow-up were retrieved. Comparisons with European norms were performed. Non parametric statistics was carried on.
**Results:** We identified 65 long-term survivors after esophagectomy and gastric pull-up for cancer. The median age was 64 years (IQR 58; 70) with a median follow-up of 4 years (IQR 3; 5). Most patients reported early satiety (76.9%), whereas dysphagia (10.8%), reflux (33.8%), regurgitation (20.0%) and dumping (24.6%) were less frequently reported. The median alimentary comfort rating was 8 of 10. Patient's global quality of life was comparable to European population values (mean 74.0 vs. 75.7, $p = 0.27$). Patients reported lower physical functioning (mean 84.5 vs. 91.0, $p = 0.005$) and more insomnia (mean 19.0 vs.15.7, $p = 0.005$) and appetite loss (mean 9.7 vs. 4.8, $p = 0.01$) than European population.
**Conclusion:** Long-term survivors after esophagectomy for cancer had a global quality of life comparable to the European population. Alimentary satisfaction was good but appetite loss and early satiety were reported even at long term. Such results enhance the importance of long-term follow-up in EC evaluating alimentary and functional aspects in addition to recurrence surveillance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0228 PROSPECTIVE RANDOMISED STUDY COMPARING BILLROTH II WITH BRAUN ANASTOMOSIS VERSUS ROUX-EN-Y RECONSTRUCTION AFTER RADICAL DISTAL GASTRECTOMY

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**Introduction:** Billroth II reconstruction is the most common method of reconstruction after distal gastrectomy because of its simplicity. However, enterogastric reflux is regarded as an unavoidable consequence of this procedure. Enterogastric reflux of bile acids leads to reflux gastritis and esophagitis. Apart from morphologic changes, enterogastric reflux causes various symptoms

**Abstract No: P0228**

| | | RY(n = 14) | BEE(n = 13) | p value |
|---|---|---|---|---|
| Residual food | Grade0 Grade1 Grade2 Grade3 Grade4 | 10(71.4%) 2(14.3%) 2(14.3%) 0 0 | 12(92.3%) 0 0 1(7.7%) 0 | 0.07 |
| Degree of gastritis | Grade0 Grade1 Grade2 Grade3 | 7(50%) 7(50%) 0 0 | 1(7.7%) 7(53.8%) 5(38.5%) 0 | **0.003** |
| Extent of gastritis | Grade0 Grade1 Grade2 Grade3 | 7(50%) 0 7(50%) 0 | 1(7.7%) 3(23.1%) 7(53.8%) 2(15.4%) | **0.008** |
| Bile reflux | Present Absent | 0 14(100%) | 12(92.3%) 1(7.7%) | **< 0.0001** |

$p < 0.05$ is significant

that adversely affects the quality of life of the patients after distal gastrectomy. There is still controversy regarding which is the best method of reconstruction after radical distal gastrectomy and how factors like bile reflux and other consequences of different types of reconstruction influence the postoperative quality of life. Therefore, a prospective randomized study has been undertaken to evaluate incidence of bile reflux, reflux gastritis, reflux esophagitis, postoperative quality of life according to reconstruction method after radical distal gastrectomy for gastric cancer and to find out the best method.

**Aims & Methods:** The aim of this study is to compare Billroth II with Braun anastomosis (BEE) and Roux-en-Y gastrojejunostomy (RY) after radical distal gastrectomy for gastric cancer in terms of bile reflux, endoscopic and histologic changes in the gastric remnant and postoperative outcomes in terms of morbidity, mortality and quality of life. The study was conducted from June 2012 to November 2013 at Department of Surgical Gastroenterology, Sri Venkateswara Institute of Medical Sciences, Tirupati, India.

**INCLUSION CRITERIA:** 1. Patients with histopathologically confirmed adenocarcinoma of the distal stomach suitable for radical distal gastrectomy with curative intent. 2. Age between 21–80 years.

**EXCLUSION CRITERIA:** 1. Patients not willing to participate in the study 2. Patients who have undergone previous gastric surgery. 3. Patients with previous small bowel surgery precluding construction of either form of anastomosis. 4. Patients operated for palliation of gastric outlet obstruction, bleeding and perforation. 5. Patients who underwent additional organ resection. The study was approved by the Institutional Research Approval Committee and Ethical Committee. All participants gave informed consent before enrollment in the study.

**Results:** The mean age of patients in RY group was 54.57 years and in BEE group was 54.08 years. Comparison of two groups based on reconstruction type showed significant differences in the incidence of bile reflux on endoscopy. None (0/14) of the patients who underwent RY reconstruction showed evidence of bile reflux on endoscopy. One patient (1/13) in the BEE group showed evidence of bile reflux on endoscopy. The frequency of bile reflux was significantly lower in the RY group (7.1%) than in the BEE group (46.1%) based on the hepatobiliary scintigraphy ($p = 0.03$) Two patients (2/14) in the RY group and one patient (1/13) in the BEE group were found to have stomal ulcer on follow up. The remnant stomach after Billroth II with Braun anastamosis showed significantly more severe and extensive gastritis than after Roux-en-Y gastrojejunostomy when visualised during endoscopy. None of the patients in both the groups had evidence of reflux esophagitis on endoscopy. The symptom scores based on quality of life questionnaire were comparable between the two groups at 3 months follow-up. **Comparison of endoscopic findings in remnant stomach after each type of reconstruction**.

**Conclusion:** In our study, Roux-en-Y reconstruction is superior to Billroth II with Braun anastomosis comparing reflux by endoscopy and hepatobiliary scintigraphy and endoscopic severity of gastritis. However, there is no difference in quality of life between these reconstruction methods at 3 months follow-up.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0229 COMPARISON OF SHORT TERM OUTCOMES FOLLOWING TOTALLY LAPAROSCOPIC AND LAPAROSCOPIC ASSISTED DISTAL GASTRECTOMY FOR GASTRIC CANCER


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**Introduction:** Laparoscopic-assisted distal gastrectomy (LADG) has been common procedure for early gastric cancer. And totally laparoscopic distal gastrectomy (TLDG) is regarded as a difficult method due to technical problems. However, instruments have evolved and operators have become proficient. Recently, advantage of TLDG has been reported by several institutions.

**Aims & Methods:** This study aimed to compare the short-term surgical outcomes of patients with gastric cancer undergoing TLDG to those of patients undergoing LADG. A total of 232 gastric cancer patients who underwent LADG (115 patients) or TLDG (117 patients) with lymphadenectomy from March 2010 to February 2016 were retrospectively studied from a prospectively designed database.

**Results:** Operating time for TLDG group ($245 \pm 38$ min) was significantly shorter than for LADG group ($278 \pm 70$ min) ($P < 0.001$). Blood loss during surgery was less for TLDG ($77 \pm 29$ ml) than for LADG ($128 \pm 65$, ml) ($P < 0.001$). There was no significant difference between TLDG and LADG with regard to postoperative hospital stay, first flatus passage and start of soft diet. Although number of total retrieved number was much larger in TLDG ($49 \pm 18$) than LADG ($42 \pm 15$), adequate lymphadenectomy was performed in both groups. Postoperative morbidity rates in TLDG and LADG were similar (5.9% vs 9.5%, $P = 0.757$). Postoperative pain scores were 4.2 vs 4.3, 3.4 vs 3.4 and 2.4 vs 2.5 at postoperative days 1, 3, and 5 respectively in the TLDG and LADG. ($P = 0.932$, 0.804 and 0.440).

**Conclusion:** This study suggests that TLDG is technically safe and feasible procedure as LADG and better cosmetic procedure for the treatment gastric cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0230 EFFICACY OF ORAL VITAMIN B12 SUPPLEMENTATION AFTER TOTAL GASTRECTOMY – RESULTS FROM A PROSPECTIVE STUDY


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**Introduction:** Vitamin B12 (vitB12) deficiency is a common and early complication after total gastrectomy which may be associated with megaloblastic anemia and neurologic symptoms potentially irreversible. Intramuscular injection of vitB12 has been considered the standard treatment, however, it is painful, expensive and, currently, difficult to obtain in our country.

**Aims & Methods:** We performed a prospective uncontrolled study (ACTRN12614000107628) in order to evaluate the laboratorial and clinical efficacy of long-term oral vitB12 supplementation in patients who underwent total gastrectomy (primary outcome). The secondary outcome was to evaluate other nutritional deficiencies namely iron and folate deficiency. All patients received daily oral vitB12 (dosage: 1 mg/day) and were evaluated every 3 months (clinical and laboratory evaluation: haemoglobin, vitB12, total iron, ferritin and folate). Statistics: SPSS 23 (Wilcoxon test).

**Results:** A total of 26 patients were included in this study, mean age of 64 years (29–79), with the diagnosis of adenocarcinoma ($n = 25$) and MALT lymphoma ($n = 1$). Patients were included 65 months after total gastrectomy (3-309). At inclusion time, 17/25 patients were under intramuscular vitB12 and 8 had not yet started supplementation. There were normal serum levels of vitB12 in 25/26 patients (1/26 with low vitB12 levels due to non-adherence to intramuscular supplementation) - mean vitB12 level of 657 pg/ml (136–2642). During the follow-up, all patients had normal vitB12 levels, and there was no need of intramuscular therapeutic. The patient with low vitB12 serum levels had an increase to adequate levels, which maintained stable. There were no differences with statistical significance among vitB12 levels at 6 (867 pg/ml), 12 (1008 pg/ml) and e 24 (1061 pg/ml) months, although there was a progressive increase of them. Iron and folate supplementation was necessary in 12 and 7 patients, respectively.

**Conclusion:** Oral vitB12 supplementation is effective and safe in patients who underwent total gastrectomy and should be considered the preferential form of supplementation in this group of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0231 SEXUAL DISORDERS AFTER LOW ANTERIOR RESECTION OF THE RECTUM

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**Introduction:** Low anterior resection of the rectum is a treatment of choice in patients with diagnosed low rectal cancer. Surgical resection of the rectum can result in multiple complications related to lesion of neighbouring neural structures responsible for fecal continence as well as urinary and sexual function.
**Aims & Methods:** In our study we investigate the sexual disorders in patients who underwent a low anterior resection of the rectum. The sexual activity, comfort of the experience, quality of sexual life during 3 periods: before surgery, a month after and half a year after were analyzed. Analysis of comorbidities, previous surgeries and trauma as risk factors of sexual disorders. Patients with rectal cancer who underwent low anterior resection of the rectum at the Department of General and Colorectal Surgery at the Medical University in Lodz during the period from 2003 to 2015 were asked to complete a questionnaire concerning their sexual activity before and after surgical procedure. The questionnaire was comprised of 37 closed-ended questions. Only fully completed questions (surveys) were included to further statistical analysis.
**Results:** The study analysis involved 100 fulfilled questionnaires – 43 women and 57 men. Patients mean age was $56.9 \pm 7.6$. A statistical, significant differences between the periods of time (before surgery, month after surgery and half year after surgery) and quality of sexual life was noted ($p < 0.001$). No relationship was found between the sex of patients and quality of their sexual life. However, the quality of sexual life one month after the surgery was significantly lower in patients with diagnosed hypertension ($p = 0.009$).
**Conclusion:** Low anterior resection (of rectum) significantly impairs the sexual activity of patients. However, these disorders are passing of over time. Also LAR procedures have strong negative impact on fecal, gas and urinary incontinence which may, in addition, intensify sexual discomfort.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0232 OUTCOME PREDICTORS AND TREATMENT OF BILIARY COMPLICATIONS POST LIVER TRANSPLANTATION

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**Introduction:** Liver transplantation (LT) can be life saving for the patient with acute liver failure and end-stage liver disease. However, LT is associated with significant morbidity and mortality. Biliary complication (BC) is one of the major causes of morbidity among LT recipients.
**Aims & Methods:** We aim to investigate the outcome predictors and treatment of BC post LT. Patients with LT performed from 2005–2015 were prospectively monitored for BC. Diagnosis of BC was made by cholangiography (MRCP, ERC or T-tube cholangiography). Cases were censored at death or last follow up. Kaplan Meier curves were used to present survival data. Analyses were performed using Cox-regression or logistic binary regression. Statistical analysis was performed with SPSS 21.0.
**Results:** Total of 81 consecutive LT patients were included. Total follow-up duration was 4086 patient-months. Median age was 61.5 years and 69.1% were males. Etiology of underlying liver disease of LT patients included hepatitis B (42%), autoimmune liver diseases (14%), cryptogenic (12%), alcohol (10%), hepatitis C (9%) and others (13%). Deceased donor liver transplant (DDLT) and living donor liver transplant (LDLT) were 71.6% and 28.4% respectively. BC was diagnosed in 30.9% of LT patients (21 strictures, 7 leaks and 2 choledocholithiasis and 1 sphincter of Oddi dysfunction). BC was associated with worse 5-year patient survival (84% vs 58%, $p = 0.013$). Surveillance ultrasound missed 57.1% of biliary strictures, which were subsequently confirmed on MRCP or cholangiography. Among patients with biliary strictures, 81% had anastomotic strictures (AS) and 19% had non-anastomotic strictures (NAS). All AS were treated with ERC and stenting with or without balloon dilatation. Majority (80%) of AS achieved complete resolution of stricture after an average of 5.0 ERC over median intervention period of 16.8 months. Of those who had not achieved complete resolution, 3 were still undergoing 3-monthly ERC and 2 had died from non-BC-related causes prior to treatment completion. There was no recurrence of strictures in those who had achieved complete resolution. Complications from ERC were low [cholangitis (1.33%) and bleeding (1.33%)]. Factors associated with the development of BC were longer cold ischemia time of more than 6 hours ($HR = 4.45$, $p = 0.015$) and LDLT ($HR = 4.5$, $p = 0.004$). Predictors of poor outcomes in patients with biliary strictures were elevated serum alkaline phosphatase (ALP) more than 581U/L ($OR = 4.9$, $p = 0.044$) and presence of NAS ($OR = 32.5$, $p < 0.01$).
**Conclusion:** We found that factors associated with development of BC post liver transplant are LDLT and prolonged cold ischemia time. ERC with stenting is a safe, effective and durable treatment option for anastomotic strictures. Predictors of poor survival in patients with BC post LT are elevated serum ALP at diagnosis and presence of non-anastomotic strictures.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0233 EMERGENCY LAPAROTOMY: STRATEGIES TO ACHIEVE INTERNATIONAL BENCHMARKS IN LOW - MIDDLE INCOME COUNTRIES (LMIC)

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**Introduction:** Advancements in surgical techniques and critical care over the last 2 decades have led to a low mortality of ≤5% for major elective digestive tract surgery. Similar results have however not been replicated for major emergency laparotomy (EL) where the current mortality ranges between 15 – 20% in best of healthcare systems.[1, 2] A recent review reported that while LMIC carry majority burden of emergency conditions they have only a limited capacity to deal with the problem.[3].
With an aim to achieve prevalent international benchmarks, we introduced a series of steps for an efficient conduct of EL. The outcome was evaluated in terms of morbidity, mortality and costs.
**Aims & Methods:** Intervention: EL.
Period: December 2012 – December 2015.
Study design: Retrospective.
Patients: >16 years, Consecutive.
Exclusions: Laparoscopic surgery.
Setting: Tertiary care referral hospital.
Modifications:.
- All patients admitted to ICU for preoperative stabilization (intravenous fluids and antibiotics) and maintained until postoperative optimization.
- Preferred radiologic investigation: Abdominal computed tomography scan.
- All imaging was evaluated by senior radiologist.
- All operations performed by team of senior digestive tract surgeons.
- A senior internist well versed with critical care issues was an integral part of the team.

Outcome measures: 30 – day mortality, morbidity, re-admission and costs.
**Results:** Of the 102 patients there were 62 males & 40 females with median age of 60 (range 16 -93) years. The indications for surgery included obstruction 30, perforation 27, acute ischemia 16, gastrointestinal bleed 10, and others 19.
There were no complications in 22 (21.5%) patients while Clavien – Dindo complications grade I & II occurred in 48 (47%) patients. Complications ≥III occurred in 31.3% patients [III (2.9%), IV (9.8%) and grade V in 19 (18.6%) respectively]. The 30 day readmission rate was 8 (7.8%). The overall median length of stay was 10 (range 2 – 72) days.
The median all inclusive cost of treatment was INR 379.255 /- (Approximately €5000). For patients with no complications or outcomes Clavien – Dindo grade I-II, the median cost was INR 318.483 (range 121.344/- to 11, 65.429/-), approximately €4201. For patients in grade III, IV & V the median cost was INR 710500/ (range 147081 – 32, 000, 00/-), approximately €9373.
At step wise logistic regression analysis serum albumin ≤2 gm% ($P < 0.0001$) and multiorgan failure ($P = 0.002$) were independent predictors of mortality.
**Conclusion:** With careful preoperative planning, optimal use of available resources and minimizing complications, EL can be performed at LMIC centers with outcomes consistent with prevalent international benchmarks and at affordable costs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0234 OUTCOME, COMORBIDITY, HOSPITALIZATION AND 30-DAYS MORTALITY AFTER PERFORATION CLOSURE BY THE OVER-THE-SCOPE-CLIP (OTSC) IN AN UNSELECTED COHORT OF PATIENTS

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**Introduction:** Acute gastrointestinal defects contain a high risk of morbidity and mortality and may be closed endoscopically by a full-thickness over-the-scope clip (OTSC).
**Aims & Methods:** Unselected consecutive patients presenting with acute non-surgical or postoperative perforations underwent attempted OTSC placement as primary closure method after interdisciplinary consensus in three tertiary referral centers. Their clinical data and intervention characteristics were evaluated in an intention to treat analysis during a 24 months period to assess closure rates, 30-days mortality, hospitalization and comorbidity.
**Results:** In total, 34 patients (16 female, 18 male, 69.5 years) were included with 22 non-surgical perforations and 12 postoperative perforations. Definitive closure of perforation was achieved in 26/34 patients (76.5%). Successful perforation closure resulted in a significantly shorter hospital stay (8 days, $p = 0.03$) and was significantly correlated with comorbidity ($r = 0.56$, $p = 0.005$). In the group with OTSC failure hospitalization was 18 days and 6 of 8 patients (75%) required immediate surgery. Three deaths occurred in the group with successful perforation closure due to comorbidity, while one death in the OTSC failure group was related to a refractory perforation. Favorable indications and locations for a successful OTSC procedure were identified as PEG complications, endoscopic or postoperative perforations of stomach, colon or rectum, respectively.
**Conclusion:** In unselected patients OTSC was effective for closure of acute perforations in more than 75% of all patients. Clinical success and short hospitalization were best achieved in patients without comorbidity, but perforation closure was found to be not the only parameter relevant for patient outcome and mortality.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0236 LONG TERM QOL AFTER ESOPHAGECTOMY: DO POST-OPERATIVE COMPLICATIONS MATTER?

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**Introduction:** Esophageal cancer (EC) is the eighth most common cancer in the world; despite new advances in neoadjuvant therapies, the outcome remains poor compared to other malignancies. The surgical resection plays a key role but it is still burdened by high rate of complications even in tertiary referral centers. Health-related quality of life (HRQL) is one of the most important outcome measure to determine how the disease and its treatment affect patient's daily life. Few data are known about the impact of surgical complications after esophagectomy on HRQL.
**Aims & Methods:** The aim of this study was to analyze the impact of surgical complications after esophagectomy for cancer on HRQL of patients with at least one year follow-up postoperatievely. Patients were prospectively enrolled in two tertiary referral centers (one in The Netherlands and one in Italy). Quality of life was evaluated using the Dutch and Italian version of the EORTC QLQ-C30 and OG25. Data about patients' characteristics, treatment and follow-up were retrieved from the centers'prospective databases. Perioperative complications were classified using the Clavien-Dindo classification of surgical complication. Patients were further matched for site of anastomosis, age, sex, AJCC stage and timing of the procedures. Non parametric statistics was carried on; data were adjusted for age, timing and center of enrollment.
**Results:** 152 patients (76 in each center) were enrolled in the outpatient clinics from October 2014 to December 2015. The median age was 62 years (IQR 55; 67); 108 (71.6%) were male and the median follow-up was 45 months (IQR 27, 58). 27 (17.8%) patients underwent esophagectomy with cervical anastomosis, 125 (82.2%) had an intrathoracic anastomosis. At univariate analysis, complication scale was directly correlated with more reflux symptom ($r = 0.185$, $p = 0.034$) and trouble with talking ($r = 0.261$, $p = 0.002$) but at multivariate analysis it did not result to be an independent predictor of worse HRQL. No differences were seen in HRQL between the two groups with the exception of anxiety which seems to affect more Italian patients than Dutch patients ($p = 0.001$).
**Conclusion:** Surgical complications after esophagectomy still affect the perioperative survival rate but, in the long run, they do not affect HRQL. Cross cultural differences showed a higher anxiety in Italian patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0237 ELECTRICAL STIMULATION THERAPY OF THE LOWER ESOGHAGEAL SPHINCTER IN TREATING GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN, OPEN LABEL PROSPECTIVE TRIAL

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**Introduction:** Electrical stimulation therapy (EST) of the Lower Esophageal Sphincter (LES) is a new treatment for Gastroesophageal reflux disease (GERD) that was always used in adult patients, in this work we describe the first two cases in children with GERD, treated with EST, the device improves the pressure of the LES without interfering with its relaxation.
**Aims & Methods:** To describe the fist two cases in pediatric population with the use of ENDOSTIM, shows an alternative in the treatment of GERD by electrical stimulation. Case 1: Female, 12 years old with GERD, with chronic pain, semi choking episodes, heartburn, regurgitation which does not respond to proton pump inhibitors with abnormal esophageal pH Demeester score of 63.2, hiatal hernia less than 3 cm and esophagitis los angeles grade C evaluated by endoscopy and biopsies reporting chronic esophagitis, manometry with pressure at rest 10.1 mmHg (normal up 14), complete relaxation, the mother refused performing Nissen fundoplication, the case was evaluated and approved by the Bioethics Committee of the hospital. Case 2: Male, 2 years old with GERD, down syndrome, weight 9.1 kg, growth and with failure, aspiration pneumonia because of gastroesophageal reflux, with no response to proton pump inhibitors for about a year, endoscopy with los angeles grade c esophagitis, pathology with reflux esophagitis, pH metry with 95% acid reflux, manometry relax pressure 10 mmHg. Two Bipolar stitch electrodes were placed in the LES using laparoscopy and a dispositive was placed in a subcutaneous pocket, electrical stimulation was delivered at 20 Hz, 215 ns, 3–8 mA, in 30 minutes session, with recess of 90 minutes, without chance of this parameters, the patient was evaluated using GERD daily symptom and medication use, endoscopy, esophageal pH and high resolution manometry.
**Results:** 1 female patient, on chronic acid-suppresive therapy who underwent successful laparoscopic implantation of the LES stimulation system, 2 weeks after the surgery the patient reported better symptom control without the intake of PPI, and the absence of heartburn and regurgitation. 1 month follow-up with esophageal pH shows decrease of Demeester score to 20.2, and 3 months esophageal pH shows decrease to 3.9, manometry with primary peristalsis in 80% of swallowing, complete relaxation, pressure at rest EEI 16.9 mmHg, endoscopy with biopsies reported esophagitis los angeles grade A, 6th postsurgical month pH Demeester index 9, manometry pressure at rest EEI 33, normal endoscopy. 1 male patient, adequate laparoscopic implantation of LES stimulation system, 1 week after the surgery the patient has a normal feeding, decrease in symptoms, 3 weeks post surgical weight increase 900 grs., first post surgical month pH metry Demeester index 6, 28% of acid reflux, with improvement in their quality of life, 3rd post surgical month endoscopy los angeles grade a esophagitis, pH 12% acid reflux, manometry pressure at rest EEI 17 mmHg.
**Conclusion:** These are the first two pediatric case in the world with electrical stimulation as a treatment for GERD; the results show that electrical stimulation of the LES can improve symptoms of GERD, reduce esopagheal acid exposure by augmenting esophageal sphincter pressures and reduce the need for PPI medication without Gastro esophageal side effects typically seen with other antireflux procedures that involve mechanical alteration of the gastroesophageal junction. Formal randomized clinical trials are needed; this will test the true rate of operative complication and side effects, and the studies could assess whether the device is restricted to patients with no hernia or is suitable for use after crural repair to know the real benefit and safety of this study.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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MONDAY, OCTOBER 17, 2016 10:30–17:00
**IBD I – POSTER EXHIBITION**

## P0238 VOLUNTARY EXERCISE IMPROVES THE HEALING OF EXPERIMENTAL COLITIS IN MICE FED DIET-INDUCED OBESITY. ESSENTIAL ROLE OF ENDOCRINE FACTORS RELEASED FROM SKELETAL MUSCLES AND ADIPOSE TISSUE

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**Introduction:** Inflammatory bowel diseases (IBDs) are a heterogeneous group of disorders which exhibit two major phenotypic forms, Crohn's disease (CD) and ulcerative colitis (UC), characterized by a cyclical nature, alternating between active and quiescent states impairing the patients' quality of life. Although progress has been made in understanding of IBD, their etiology is unknown but several factors from adipose tissue and skeletal muscles such as cytokines, adipokines and myokines were implicated in the pathogenesis of IBD. The hypertrophied mesenteric white (mWAT) adipose tissue was shown to increase the circulating proinflammatory cytokines that predisposed to development of colitis. Among therapeutic options, exercise was proposed as one of the most important lifestyle practices to adopt when considering treatment options for IBD but mechanism of this beneficial effect of voluntary endurance training in amelioration of lower bowel disorders has not been extensively studied.
**Aims & Methods:** We determined whether diet-induced obesity (DIO) augments the severity of experimental colitis in C57mice and whether moderate exercise can affect the experimental colitis induced in DIO mice. The effect of voluntary physical activity on the changes in colonic blood flow (CBF) and the plasma myokine irisin released from exercising muscles and plasma adiponectin levels from adipose tissue, and the concentrations of plasma proinflammatory cytokines in DIO mice with colitis were investigated. Ninety mice were randomized into two series A and B and fed with 70% fat diet (cholesterol up to 70%, Altromin, Lage, Germany, series A) and with normal diet (ND, series B) and subjected to the voluntary wheel running to assess the effect of physical performance and endurance on the healing of colitis. For endurance test, mice individually housed were allow to run freely on the open surface wheel placed outside a standard mouse cage. Rotations were electronically transmitted to a USB hub so that frequency and rate of running was captured via a software program for data storage and analysis for variable time periods. After 6 weeks of wheel exercise, colitis was induced in both series of mice A and B by intra-colonic administration of TNBS. The severity of colonic damage (DAI index), the alterations in the colonic blood flow (CBF) determined by $H_2$ -gas clearance technique in colonic mucosa, the plasma concentration of TNF-$\alpha$ and IL-1$\beta$, adiponectin, leptin, IL-6, TWEAK and irisin were assessed by ELISA.
**Results:** The macroscopic and microscopic colitis in sedentary ND mice was accompanied by the significant fall in the CBF, an increase in colonic tissue weight and significant increase in the plasma IL-1$\beta$ and TNF-$\alpha$ levels ($p < 0.05$). In sedentary mice fed DIO, the colonic lesions and the colonic tissue weight were aggravated and the plasma IL-1$\beta$, TNF-$\alpha$, TWEAK and leptin levels were significantly increased ($p < 0.05$) but a significant decrease in plasma irisin and adiponectin levels ($p < 0.05$) were observed comparing to non-exercising ND mice. Exercise of DIO rats significantly decreased the severity of TNBS-induced colonic damage while significantly increasing the CBF and attenuated the increase in plasma IL-1$\beta$, TNF-$\alpha$, TWEAK, and leptin levels. Wheel running significantly increased plasma levels of myokines IL-6 and irisin but this enhancement failed to reach the rise in plasma of these cytokines observed in ND fed mice ($p < 0.05$). These changes in plasma levels of proinflammatory markers IL-1$\beta$, TNF-$\alpha$, TWEAK and leptin were rather moderate in ND fed animals and further significantly decreased by exercise.
**Conclusion:** 1) The healing of experimental colitis is impaired in mice fed DIO and this effect is mediated by a fall in colonic microcirculation and an increase in plasma proinflammatory markers such as IL-1$\beta$, TNF-$\alpha$, IL-6 and TWEK; 2) voluntary physical activity can diminish of the severity of colonic damage in DIO fed mice mediated, at least in part, by a release of myokines such as protective irisin, and 3) regular voluntary exercise could exert a beneficial effect in IBD by affecting abdominal adiposity due to restoration of protective adiponectin and promotion of anti-inflammatory environment by inhibition of proinflammatory cytokines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0239 EICOSAPENTAENOIC ACID-FREE FATTY ACID SUPPLEMENTATION FOR THE PREVENTION OF COLITIS-ASSOCIATED COLORECTAL CANCER: A PHASE-I CLINICAL TRIAL

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**Introduction:** Long-standing ulcerative colitis (UC) patients are at highrisk of developing colitis associated colorectal cancer (CAC). We have previously demonstrated that EPA-FFA protects towards CAC in the AOM-DSS mouse model through modulation of the Notch1 signaling and gut microbiota.
**Aims & Methods:** To expand our previous findings, in this study we evaluated whether the treatment with Eicosapentaenoic acid-free fatty acid (EPA-FFA) was able to affect markers associated with CAC progression in UC patients. 20 long-standing UC patients in stable clinical remission (SCCAI = 0) and with fecal calprotectin (FC) > 150 µg/g measured in stools were recruited and treated with 2 g/day of EPA-FFA (ALFA, SLA Pharma AG, Switzerland) for 90 days. Biopsies and biological samples were collected at the entry (T0) and at the end of the study (T3). Compliance was evaluated by EPA incorporation into red blood cell membranes. Protein levels of Jagged1, Hes1, Stat3, phospho-Stat3 and Klf-4 were determined by western blotting. IL-22, IL-10 and SOCS3 mRNA levels were analyzed by qRT-PCR. Goblet cells were stained by Alcian blue. Microbiota analyses were performed on fecal and biopsies DNA samples sequencing the V3-V4 region of the bacterial 16S rRNA gene; as a reference, we employed a healthy adult population previously analyzed for microbiota composition. Endoscopic and histologic disease activities were measured by Mayo and Geboes scores respectively.
**Results:** 19 patients completed the study; 17 patients resulted adherent to treatment based on EPA levels at T3 with an overall compliance of 89.5%. Patients showing clinical, histological or endoscopic reactivation at T3 (n = 3) were considered as non-responders. The per-protocol analysis, conducted on patients incorporating EPA and which did not show any sign of disease at T3 (n = 15), demonstrated that EPA-FFA treatment induced IL-10 and SOCS3, partially inhibiting STAT3 activation. Moreover, we observed a concomitant significant induction of Hes1 and Klf-4 associated with goblet cells differentiation. Importantly, some dysbioses associated with UC at T0, were partly redressed by the EPA-FFA treatment. In particular, EPA-FFA treatment increased the abundance of fecal Prevotellaceae and Porphyromonadaceae families and decreased mucolytic Bacteroides spp at mucosal level.
**Conclusion:** EPA-FFA supplementation promotes intestinal homeostasis in patients with long-standing UC inducing goblet cells differentiation, limiting STAT3 activation through the modulation of IL-10/SOCS3 axis and contributing to restore intestinal eubiosis. Overall, our data suggest a protective role of EPA-FFA on CAC onset during UC.
*The two first authors equally contributed to this work.
**Disclosure of Interest:** L. Ricciardiello: Luigi Ricciardiello has received an unrestricted scientific grant from SLA Pharma AG.
All other authors have declared no conflicts of interest.

## P0241 ALTERATION IN MICROBIOTA COMPOSITION CONTRIBUTES TO CHRONIC INFLAMMATORY RESPONSE TRIGGERED BY CROHN'S DISEASE-ASSOCIATED AIEC INFECTION IN GCN2 DEFICIENT MICE

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**Introduction:** A high prevalence of the adherent-invasive *E. coli* (AIEC) in the intestinal mucosa of Crohn's disease (CD) patients has been shown. We previously showed that AIEC persist in the intestine and induce inflammation in transgenic CEABAC10 mice expressing human CEACAM6, the receptor for AIEC. We also showed that upon infection, autophagy is induced in host cells to restrain AIEC intracellular replication and that this requires activation of the GCN2/eIF2alpha/ATF4 pathway. Autophagy response upon AIEC infection was inhibited in *gcn2*$^{-/-}$ mice, leading to increased AIEC colonization and AIEC-induced inflammation. Here, we investigated whether transient AIEC colonization of mice deficient for Gcn2 induces changes in the gut microbiota, which might contribute to the development of chronic inflammation.
**Aims & Methods:** Wild type (WT) and *gcn2*$^{-/-}$ mice, or transgenic CEABAC10 invalidated for Gcn2 (CEABAC10/*gcn2*$^{-/-}$) or not (CEABAC10/*gcn2*$^{+/+}$) were infected with the AIEC reference strain LF82 or the non-pathogenic *E. coli* MG1655 strain by gavage. Feces were collected at different time points and used to determine AIEC persistence, to quantify the amounts of the inflammatory marker lipocalin-2 and to analyse microbiota composition by 454

pyrosequencing. The microbiota analysis data were analysed using Quantitative Insights Into Microbial Ecology (QIIME) software package.
**Results:** In WT and *gcn2*$^{-/-}$ mice, LF82 colonization was higher and lasted longer compared to the colonization of MG1655. However, LF82 was undetectable in the feces of mice at day 4 post-infection, indicating that in this model of infection, in which neither a cocktail of antibiotic nor DSS was used, the gut colonization by AIEC was transient. The microbiota analyzed by UniFrac metrics and principal coordinates analysis (PCoA) did not show any pattern of clustering or significant change at the family level in WT mice upon LF82 infection. However, for the LF82-infected *gcn2*$^{-/-}$ mice, PC analysis showed a clear pattern of clustering at day 14 and 21 post-infection. This was associated with significant changes at the family level with an increase in *Bacteroidetes* and *Proteobacteria* and a decrease in *Firmicutes*. These changes are consistent with those observed in CD patients. Furthermore, lipocalin-2 levels were increased in LF82-infected *gcn2*$^{-/-}$ mice at day 21 post-infection compared to other groups of mice. These data showed that chronic intestinal inflammation was developed in *gcn2*$^{-/-}$ mice after AIEC clearance and more importantly after the modification in the microbiota composition. Finally, the results obtained for CEABAC10/*gcn2*$^{-/-}$ mice were consistent with those obtained for *gcn2*$^{-/-}$ mice.
**Conclusion:** Herein, we show that, in genetically predisposed hosts, a transient colonization of a pathobiont AIEC strain could lead to a change in the gut microbiota that persisted even after AIEC clearance. Furthermore, this change in the microbiota seems to contribute to the development of a chronic inflammation response as observed in CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0242 ANTI-INFLAMMATORY AND ANTIBACTERIAL EFFECTS OF HUMAN CATHELICIDIN ACTIVE FRAGMENT KR-12 – A NOVEL POTENTIAL THERAPY OF INFLAMMATORY BOWEL DISEASE

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**Introduction:** Inflammatory bowel diseases (IBD), which consist mainly of Crohn's disease (CD) and ulcerative colitis (UC) is a group of gastrointestinal tract diseases with uncertain etiology. Several therapeutic options are used in IBD; the choice of the treatment depends on disease activity, behavior and extent. Analogs of 5-aminosalicylic acids (5-ASA) administered orally or rectally are first-line drugs. Glucocorticoids, anti-inflammatory agents and biologicals are used when remission has not been achieved. In portion of patients none of the available therapies is effective and surgical intervention is necessary. Therefore novel pharmacological treatment options are still sought in order to avoid the disabling procedures. Cathelicidins derive from a family of antimicrobial peptides (AMPs). In addition to their potent anti-pathogenic ability, they exhibit chemotactic, immunomodulatory and angiogenic properties [1]. The sole human representative of cathelicidins, LL-37, was found to be potentially implied in the pathogenesis of IBD [2]. Currently, shorter analogues of LL-37 are under development.
**Aims & Methods:** In our study, we attempted to assess the anti-inflammatory and antibacterial actions of LL-37 and its shortest fragment, KR-12 (both 1–5 mg/kg, i.p., twice daily) in two mouse models of colitis: induced by 2, 4, 6-trinitrobenzenesulfonic acid (TNBS) and dextran sulfate sodium (DSS). The extent of inflammation was evaluated based on the macroscopic score, quantification of myeloperoxidase (MPO) activity and microbiological analysis of stool samples.
**Results:** The results of a preliminary study with low doses of LL-37 and KR-12 showed a non-significant decrease in macroscopic score and ulcer score in the acute TNBS model of colitis. Overall, the anti-inflammatory effect of KR-12 was more pronounced than that of LL-37; hence, further studies were performed exclusively with KR-12. In the semi-chronic TNBS model, the peptide at the dose of 5 mg/kg (i.p., twice daily) significantly reduced macroscopic score ($p < 0.05$) and ulcer score ($p < 0.001$). Furthermore, qualitative and quantitative changes in colonic microbiota were observed. In the semi chronic model of colitis induced by DSS, KR-12 significantly attenuated intestinal inflammation as demonstrated by a significant reduction in macroscopic score ($p < 0.05$) and a decrease in stool score and MPO activity.
**Conclusion:** We demonstrated potential ability of KR-12, a fragment of human cathelicidin LL-37 to alleviate inflammation in the mouse models of colitis. Although we did not achieve significant reduction in all parameters, we believe our research contributes to the field of IBD treatment. We conclude that KR-12 and cathelicidins as a whole are worth being considered as a potential therapeutic option in the treatment of IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0243 ANTI-TNFA ALTERS MOTIVATIONAL PROCESSING IN CROHN'S DISEASE PATIENTS

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**Introduction:** Inflammatory Bowel Disease is linked to immune activation and increased inflammation, evidenced by increased release of TNF-a from peripheral mononuclear cells (PBMCs). This immune response is closely linked with the intensity of gastrointestinal symptoms and extra-intestinal comorbidities such as depression or anxiety. Interestingly, in a substantial proportion of patients with inflammatory bowel disease and increased TNF-a, gastrointestinal symptoms persist after lesions heal. Motivational change (decreased reward and increased loss sensitivity) is a core feature of sickness behaviour and depressive symptoms.
**Aims & Methods:** We targeted motivational brain circuitry during reinforcement learning to assess the effects of anti TNF-a therapy on depressive symptoms in patients with Crohn's Disease. We recruited 10 patients with Crohn's disease ($30.0 \pm 13.0$ yrs, 5 female, 6 ileocolonic, 2 colonic and 2 ileal disease) in stable clinical remission (CDAI < 150) following chronic anti-TNF$\alpha$ therapy (8 adalimumab/2 infliximab). 72 hours before and after anti-TNF$\alpha$ patients underwent visceral sensory testing (standardised nutrient challenge) and functional brain scanning during a reinforcement learning task, where participants experienced both rewards and losses (gaining / losing fake $10 notes). During sensory testing 600 ml of enteral feeding solution was consumed over 15 minutes while the intensity of GI symptoms was quantitated.
**Results:** Within 72 hrs after administration anti-TNF-$\alpha$ unpleasant visceral sensation during nutrient challenge (subjective fullness) was significantly reduced (22% reduction, $p < 0.031$). Motivational circuits were strongly activated by rewards and losses, including within the nucleus accumbens and primary interoceptive cortex (insula). Anti-inflammatory therapy altered activity in the brains motivational circuits during reinforcement learning, including within the nucleus accumbens and insula cortex. Importantly, across patients, depressive symptoms (Beck Depression Inventory) also correlated with drug induced changes to rewards in the right insula cortex.
**Conclusion:** Immune modulation of the gastrointestinal tract with anti-TNF$\alpha$ agents is associated with significant reduction in symptoms during a standardised nutrient challenge, and alterations in core motivational circuitry within the brain. These alterations within the right insula cortex also reflect self reported depressive symptoms before anti-TNFa. The findings suggest that systemic reductions of circulating TNF and reduced visceral hypersensitivity is translated into improved motivational functioning, improving our understanding of psychiatric comorbidities in IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0244 CO-ABUNDANCE OF AKKERMANSIA MUCINIPHILA AND FAECALIBACTERIUM PRAUSNITZII IN THE MUCOSA OF HEALTHY AND DISEASED GUT

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**Introduction:** *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*, co-inhabitants of the intestinal mucosa, have been associated with a healthy microbiota. Depletion of *F. prausnitzii* occurs in several intestinal disorders [1], while a reduction of *A. muciniphila* has only been reported in inflammatory bowel disease (IBD) [2, 3] as few studies determining its load and including several gut diseases have been done. No direct link between this two species has been reported yet, but it can be hypothesised that *F. prausnitzii* presence in the gut is influenced by acetate producers like *A. muciniphila*, because it is a required compound for its growth [4, 5].
**Aims & Methods:** The aim of this study is to determine the amount of *A. muciniphila* in healthy subjects (H) and patients with various gut disorders, and to establish whether or not there is correlation between the abundance of the two species. *A. muciniphila* load was determined by quantitative polymerase chain reaction targeting specific regions of the 16 S rRNA gene as reported previously [6] in colonic biopsies from 17 H, 23 patients with ulcerative colitis (UC), 31 with Crohn's disease (CD), 3 with irritable bowel disease (IBS) and 3 with colorectal cancer (CRC). Data were normalised to total bacterial counts. These values of relative abundances were compared by type of disease and considering relevant clinical characteristics of patients, by non parametric statistical tests. Relative abundance of total *F. prausnitzii* and its phylogroups for these patients, available from previous studies [7], were used to establish correlation between the two species.
**Results:** A reduction in *A. muciniphila* load was observed in CRC patients compared with H subjects ($p = 0.023$), whereas for the other intestinal disorders no statistically supported differences were found with respect to H subjects due to high variation within the data. Within IBD, CD patients had lower loads of this species than those with UC ($p < 0.05$). CD patients with colonic disease location

featured the lowest abundance of *A. muciniphila*. Abundance of this species was not affected by medication or activity of the disease at time of sampling. There is correlation between the abundance of *A. muciniphila* and total *F. prausnitzii* in patients with CD ($\rho = 0.386$) and CRC ($\rho = 1.000$). In CD patients, correlation between *F. prausnitzii* phylogroup I and *A. muciniphila* was observed ($\rho = 0.360$).
**Conclusion:** CRC patients featured a striking depletion of *A. muciniphila*, but further confirmation in a larger cohort is required. Differences in *A. muciniphila* load have been found between IBD patients, therefore its quantification in conjunction to *F. prausnitzii* may help to differentiate patients with CD from those with UC. Because abundances of these two species were correlated in CD and CRC patients, further studies to confirm whether or not they are influenced by similar factors in certain gut disorders would be of interest.
**Disclosure of Interest:** X. Aldeguer: X. Aldeguer is consultant from Abbvie and has received honoraria for lectures including services on speakers bureaus from abbVie and MSD.
All other authors have declared no conflicts of interest.

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### P0245 FLAGELLA EXPRESSION OF ADHERENT-INVASIVE ESCHERICHIA COLI AND BACTERIA PERSISTENCE IN THE GUT


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**Introduction:** Adherent-Invasive *E. coli* strains (AIEC) isolated from ileal lesions of Crohn's disease patients are flagellated bacteria able to invade intestinal epithelial cells and to survive within macrophages. Flagellin (FliC), major bacterial flagellum protein, is required for motility but is also recognized by innate immune receptors TLR5 and Naip5-Naip6/NlrC4/Caspase-1 leading to pro-inflammatory cytokines release. FlgM is a protein involved in the regulation of flagellar assembly. Its function is to associate flagellar assembly to appropriate temporal flagellar gene transcription.
**Aims & Methods:** In this work, we aim at better understanding if efficient modulation of flagellin expression is required for mucosa colonization and in vivo persistence, and allows AIEC to evade innate immune detection. For that, transgenic mouse model expressing human CEACAM6 (CEABAC10) was used in this study. Bacterial persistence in the colonic mucosa of mice, treated or not with dextran sodium sulfate (DSS) used to disrupt mucus layer, was measured after infection by wild-type AIEC LF82, AIEC-DfliC and AIEC-DflgM mutants.
**Results:** The abilities of the wild-type AIEC LF82, AIEC-DfliC and AIEC-DflgM mutants to colonize colonic mucosa in CEABAC10 mice model treated with DSS were analyzed. We observed at 4 days post-infection that AIEC-DfliC significantly better colonized colonic tissue (median of $3.3 \times 10^6$ bacteria/mg of tissue) than AIEC LF82 (median of $9.3 \times 10^5$ bacteria/mg of tissue). In contrast, we observed that LF82-DflgM overproducing flagellin presented a lower ability to colonize colonic mucosa than WT AIEC LF82 (median of $5.0 \times 10^5$ bacteria/mg of tissue). However, when the mucus layer was not altered by DSS treatment in CEABAC10 mice, the higher persistence of AIEC-DfliC was no longer observed. This indicates that flagella expression by bacteria allows the crossing of the mucus layer, but overexpression of flagellin in the contact of epithelial cells can be detrimental to the virulence by inducing acute inflammation enhancing AIEC clearance.
**Conclusion:** This work aims to better understand the pathogenicity of AIEC strains to develop specific inhibitors interfering with bacteria/cell interaction, and shows that flagella expression should be finely regulated for optimal virulence of AIEC pathobionts. Targeting FlgM bacterial factor could be an alternative strategy to control AIEC colonization on the gut mucosa.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0246 PROTEOMIC MARKERS OF EARLY RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS IN REMISSION


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**Introduction:** Risk stratification of subjects with inflammatory bowel disease (IBD) into those likely to relapse and those who will remain quiescent remains a significant challenge.
**Aims & Methods:** We undertook a pilot study to investigate the association of proteomic profiles during remission in ulcerative colitis (UC) and subsequent disease relapse. 61 patients with UC in clinical, endoscopic and histological remission and 17 normal controls were included. 8 UC patients had clinical relapse of UC within 6 months from the index endoscopy (Early Relapse (ER)). 43 patients had no relapse (NR) during follow-up for 3 years. Soluble protein fractions were extracted from rectal biopsies in patients with ER and NR and normal controls using an isobaric tag for relative and absolute quantitation (iTRAQ)-compatible protocol. Samples from ER ($n = 7$), NR ($n = 7$) and two separate controls (CON) ($n = 7$ in each) were pooled and labelled. Labelled peptides were analysed by hydrophilic interaction liquid chromatography coupled with tandem mass spectrometry (HILIC-MS/MS) and data reconstituted (GeneBio Phenyx). Inter-group comparisons were made using validated in-house algorithms. iTRAQ results were validated by immunoblotting on 7 pooled ER, 7 pooled and 6 external NR, and 3 external CON samples against selected target proteins following decision tree analysis (protein fold change (FC) of $\geq 2$). Relative protein expression for each dot-blotted sample was determined from its signal intensity using densitometry. Statistical significance was set as false detection rate (FDR) and p-value of $\leq 0.05$.
**Results:** 11 upregulated and 3 down-regulated proteins in ER relative to NR were identified from iTRAQ analysis. Smooth muscle contraction, cell-cell communication, signal transduction, fatty acid metabolism, lipoprotein metabolism, semaphorin interactions, EPH-ephrin signalling, and haemostasis were the possible discriminatory cellular pathways. Similarly, 7 upregulated and 3 downregulated proteins in ER relative to controls were identified from iTRAQ analysis. Metabolism of polyamines and vesicle-mediated transport were the possible discriminatory cellular pathways. Glycoprotein A33 (GPA33) ($FC = 4$, $p = .0006$ in ER vs. NR; $FC = 3.22$, $p = .0007$ in ER vs. CON) and keratin 10 (K10) ($FC = 1.94$, $p = .0002$ in ER vs. NR; $FC = 2.49$, $p < .000$ in ER vs. CON) were chosen for further orthogonal validation. Immunoblotting confirmed down-regulated GPA33 in ER vs. NR ($p = .02$) and ER vs. CON ($p = .009$), and upregulated K10 in ER vs. NR ($p = .04$), in line with iTRAQ outcomes.
**Conclusion:** Reduced GPA33 expression and increased K10 in patients with UC in remission, is associated with early relapse, compared with those who did not relapse. This has the potential for understanding the pathogenesis of UC relapse and the development of predictive tissue biomarkers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0247 ANTIBIOTIC RESISTANCE PROFILES OF ADHERENT INVASIVE E. COLI AND NON- PATHOGENIC E. COLI ISOLATED FROM CROHN'S DISEASE PATIENTS AND CONTROLS


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**Introduction:** The adherent invasive *E. coli* (AIEC) pathotype has been associated with the aetiology of Crohn's disease (CD). The use of antibiotics for the treatment of CD has shown limited efficacy. Besides, few studies have determined the susceptibility of AIEC to antimicrobials [1, 2], and one of them reported a higher frequency of multidrug resistant (MDR) strains in CD patients than in controls.
**Aims & Methods:** We aimed to compare the antimicrobial resistance profiles of AIEC and non-AIEC strains inhabiting the gut mucosa of CD patients and controls, and to depict putative mechanisms of resistance. For this purpose, we examined the resistance to 35 antimicrobials in a collection of 22 AIEC and 27 non-pathogenic *E. coli* obtained from CD patients ($N = 31$, 16 of which were AIEC) and healthy controls ($N = 18$, 6 of which were AIEC) using the Vitek®2 system, the Sensititre plates COMPAN1F, and macrodilution tests following the 'Clinical and Laboratory Standards Institute' standards. Detection of AmpC $\beta$-Lactamases was performed by disk diffusion tests and definition of plasmidic AmpC $\beta$-lactamase (pAmpC) was determined by polymerase chain reaction. Genes encoding for antimicrobial resistance were searched in the genome of 23 AIEC available in GenBank using the ARG-ANNOT tool.
**Results:** AIEC were more frequently resistant to $\beta$-lactams than non-AIEC strains, including penicillins (> 50% of AIEC were resistant), penicillins + $\beta$-lactamase inhibitors (up to 41.2%) and first and second generation cephalosporins (up to 23.5%). About the 11% of AIEC were also resistant to third and fourth generation cephalosporins whereas none of the non-AIEC was resistant. The proportion of resistant strains to other antimicrobials such as tetracyclines, aminoglycosides and quinolones was similar between AIEC and non-AIEC strains. The number of resistances to antibiotics was slightly higher in AIEC strains ($4.59 \pm 1.23$) than in non-AIEC strains ($1.93 \pm 0.68$) and AIEC were two times more frequently MDR than non-AIEC (27.3% vs 14.8%). The phenotype and genome analysis of the LF82 strain suggested the hyperproduction of the intrinsic chromosomal AmpC. The ARG-ANNOT tool allowed the identification of several genes for resistance to antimicrobial agents that included $\beta$-lactams, aminoglycosides, macrolides, phenicols, sulfonamides, tetracyclines and folate pathway inhibitors. TEM $\beta$-lactamases were detected in 7 out of 23 AIEC genomes and OXA-9 in one of them. NRG857c strain carried a plasmid with genes that confer resistance to multiple types of antibiotics (TEM-1, strA, strB, mphB, catA1, sulII, tetA, tetR, and dfrA1).
**Conclusion:** We report an association between increased antimicrobial resistance and virulence. Further studies are needed to decipher whether or not there could be a common factor implicated in AIEC phenotype and resistance to $\beta$-lactams. Antimicrobial resistance in AIEC is a matter of concern regarding the putative implication of the pathotype in CD, especially in the case of strains carrying plasmids with multiple resistances to antimicrobials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0248 HYPOXIA POSITIVELY REGULATES EXPRESSION OF THE PH-SENSING G-PROTEIN COUPLED RECEPTOR OGR1 (GPR68)

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**Introduction:** A novel family of proton-sensing G-protein coupled receptors (GPCRs), including ovarian cancer G-protein coupled receptor 1 (OGR1, also known as GPR68) has been identified to play an important role in pH homeostasis. Hypoxia is known to change tissue pH due to anaerobic glucose metabolism through the stabilization of hypoxia inducible factor (HIF)-1$\alpha$.
**Aims & Methods:** We investigated how hypoxia regulates the pH-sensing GPCR receptor OGR1 in the intestinal mucosa and associated cells. OGR1 mRNA expression in murine tumors, human colonic tissue and myeloid cells was determined by RT-qPCR. The influence of hypoxia on OGR1 expression was studied in human MM6 cells, in primary human intestinal macrophages and in the intestinal mucosa of healthy volunteers (HV) and inflammatory bowel disease (IBD) patients. Changes in OGR1 expression in MM6 cells under hypoxia were determined upon stimulation with tumor necrosis factor (TNF), in the presence or absence of NF-$\kappa$B inhibitors. In order to study the molecular mechanisms involved, chromatin immunoprecipitation (ChIP) analysis of the OGR1 promoter was performed.
**Results:** OGR1 expression was higher (2.8-fold) in tumor compared to normal murine colon tissue. Hypoxia positively regulated the expression of OGR1 in MM6 cells, primary human intestinal macrophages and colonic tissue from IBD patients compared to HV. Under hypoxia OGR1 expression increased in THP1 cells (4.76, 13.19 and 3.82 -fold) at 8, 16 and 24 h, respectively and HT29 cells (7.78 -fold) at 24 h. The expression of OGR1, but not TDAG8 was significantly increased under hypoxia at pH 7.7, 7.3 and 6.8, with a higher increase of OGR1 expression at acidic conditions. OGR1 expression levels of MM6 cells under hypoxia increased 3.2, 3.7 and 53.5 -fold at pH 7.7, 7.3 and 6.8 respectively compared to pH 7.7, normoxia. Under hypoxia, OGR1 expression at acidic pH increased more than 14 -fold compared to pH 7.7 and pH 7.3. The expression of OGR1 in biopsies taken one week after hypoxia showed a clear trend to increase in CD and UC patients when compared to control subjects. Conversely, mRNA levels of TDAG8 in CD patients, but not HV were significantly reduced at T2 and T3 after hypoxia when compared to T1, and a similar trend was shown in UC patients. In MM6 cells, hypoxia enhanced TNF-induced OGR1 expression was reversed by the inhibition of NF-$\kappa$B. In addition to the effect of TNF and hypoxia, OGR1 expression was further increased at low pH. ChIP analysis revealed that HIF-1$\alpha$, but not NF-$\kappa$B, binds to this promoter region of OGR1 24 h after hypoxia in THP1 cells.
**Conclusion:** The enhancement of TNF- and hypoxia-induced OGR1 expression under low pH points to a positive feed-forward regulation of OGR1 activity in acidic conditions, and supports a role for OGR1 in the pathogenesis of IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0249 CORRELATION BETWEEN THE PRESENCE OF BACTEROIDETES AND FAECAL CALPROTECTIN FOR THE DETECTION OF ENDOSCOPIC ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Faecal calprotectin (FC) levels correlate directly with the endoscopic activity of inflammatory bowel disease (IBD). Microbiota plays a role in the etio-pathogenesis of IBD. In this context, the presence of specific genotypes of bacteroidetes has been shown to be associated with the activity of the disease.
**Aims & Methods:** Aim of this study was to evaluate the correlation between the presence of genotypes of bacteroidetes and the FC levels in relation to the endoscopic activity of IBD. Methods: A single-center, observational cross-sectional study was designed. Consecutive patients with Crohn's disease (CD) and ulcerative colitis (UC) who attended the Endoscopy Unit of Santiago de Compostela for colonoscopy were included. Colonic biopsies were taken to characterize microbiota by using a restriction fragment length polymorphism (RFLP) analysis on PCR products targeting the 16SrRNA genes of Bacteroidetes digested with HinfI, PciI, DpnII and AciI. CF levels were measured in faecal samples with a quick test (Quantum blue) the day before starting colon cleansing for colonoscopy. Inactive UC was defined as a Mayo endoscopic score of 0. Inactive CD was defined as a SES-CD $<= 2$. Results are shown as prevalence and median, and they were analyzed by the Mann-Withney test, Spearman correlation test and multivariate lineal regression.
**Results:** 22 patients with IBD (12 CD and 10 UC) were included. Endoscopic activity was detected in 15 patients (9 CDa and 6 UCa). 7 different genotypes of Bacteroidetes called N1, C1-C5 and CB10 were detected. The presence of genotype N1 and C1 was constant in patients with active and inactive IBD, while genotype C4 was present in 82.35% of patients with UCa and CDa, and in 17.65% of patients with inactive IBD ($p = 0.009$). The median of FC was 48 in patients with inactive disease and 205 µg/g in patients with active IBD ($p = 0.019$). In patients with genotype C4 the median of CF was 205 µg/g, whereas in patients with other genotypes the median of FC was 48 µg/g ($p = 0.446$). A positive correlation was found between C4 genotype and FC levels ($r = 0.429$). After multivariable analysis, FC levels were associated with endoscopic activity (coef 473.88, $p = 0.018$) and the presence of genotype C4 in biopsies (coef 67.92, $P = 0.014$).
**Conclusion:** FC levels and genotype C4 of bacteroidetes in colon biopsies are associated with the endoscopic activity of IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0250 15-D-PGJ2 AS A NEW REGULATOR OF HEPCIDIN EXPRESSION AND ITS INVOLVEMENT IN IRON METABOLISM

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**Introduction:** The acute phase protein hepcidin, produced mainly in the liver, has been demonstrated to be a key mediator of the cytokine-induced anaemia of chronic inflammation (ACI). Prostaglandins are recognized as both pro- and anti-inflammatory lipid mediators, and have been shown to be involved in different pathogenic inflammatory pathways.
**Aims & Methods:** Our study aimed to elucidate the role of prostagladins (PGs) in iron homeostasis. Using the pro-inflammatory PGE2 and the anti-inflammatory 15-Deoxy-Delta-12-14-prostaglandin J2 (15-d-PGJ2), the latter also a known inducer of the transcription factor Nrf2, we tested whether these lipid mediators may be involved in interleukin-6 (IL-6) and oncostatin M (OSM)-induced hepcidin expression. The liver cell line HepG2 was cultivated under standard conditions and incubated for 16 hours with IL-6 (10 ng/mL) or OSM (10 ng/mL) alone or in combination with 15-d-PGJ2 (10$\mu$M). For reporter gene assays, plasmids were transfected by lipofection and luciferase activity was measured luminometrically. Quantitative real-time PCR was performed to determine mRNA expression. Proteins were detected by Western blot analysis. For gene-knockdown, HepG2 cells were transfected with Nrf2 or nontargeting siRNA duplexes according to the protocol for reversed lipofection.
**Results:** 15-d-PGJ2 (**$p < 0.01$), but not PGE2, counteracted the OSM and IL-6 induced hepcidin induction on promoter and mRNA level significantly after 16 h when coincubated with the cytokines. Treatment with 15-d-PGJ2 leads to nuclear translocation and thus activation of transcription factor Nrf2, which was confirmed by induction of Nrf2 target genes HO-1 and NQO-1 (**$p < 0.01$) on mRNA level. Compared to nontargeting siRNA transfection, a 50% Nrf2 knockdown tended to reduce the 15-d-PGJ2 inhibition of IL-6-induced hepcidin mRNA expression. In addition, 15-d-PGJ2 significantly induced ferritin and ferroportin on mRNA level in HepG2 (**$p < 0.01$), which could be significantly counteracted by knockdown of Nrf2 target gene HO-1 (*$p < 0.01$). These results points towards a key role of Nrf2-signaling in 15-d-PGJ2 mediated effects.
**Conclusion:** Our study data demonstrated an involvement of the prostaglandin 15-d-PGJ2 in the regulation of iron homeostasis. Our preliminary data also indicate that these effects may be linked, at least in part, to the transcription factor Nrf2 signaling pathway. Further research will be needed to tighten up these data.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0251 EFFECT OF CIRCADIAN DISRUPTION ON INFLAMMATORY BOWEL DISEASE ACTIVITY: AN EXPERIMENTAL STUDY ON A DSS-INDUCED MICE COLITIS MODEL

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**Introduction:** Shift work has become increasingly prevalent across a wide range of occupations. Circadian disruption, associated with shift work, has been linked to inflammatory pathologies including inflammatory bowel disease (IBD). Circadian clock genes participate in the regulation of the integrity of the epithelial intestinal barrier, a process that is linked to IBD.
**Aims & Methods:** The aim of this study was to evaluate the effect of circadian rhythm inversion on the severity of a Dextran Sodium Sulfate (DSS)-induced colitis in mice. 25 mice were divided into 4 groups: a control group without circadian inversion (C), a control group with circadian inversion (CI), a group treated with DSS 2% (DSS) and a group treated with DSS 2% with an inverted circadian rhythm (DSSI). The fecal calprotectin (FC) and the systemic inflammatory (C-RP, IL-1ß, IL-6, TNF-$\alpha$) markers concentrations were measured in the 4 groups using the ELISA technique. RT-PCR was used to measure the expression of Per2, Claudin-1and TNF-$\alpha$ in the mice's colon in the 4 groups. Histological analysis of the extracted colon tissues was also enrolled.
**Results:** FC was significantly increased in the DSS group vs. control ($89.52 \pm 20.15$ vs $44.92 \pm 14.67$ pg/ml. $p = 0.038$), and was twofold much higher in the DSSI group vs DSS. Additionally, IL-6 ($49.99 \pm 11.44$ vs $31 \pm 9.80$ pg/ml. $p = 0.032$), TNF-$\alpha$ ($2252.5 \pm 432.08$ vs $901.67 \pm 454.67$ pg/ml. $p = 0.009$) and C-RP ($8.93 \pm 1.05$ vs $4.87 \pm 0.32$ pg/ml $p = 0.001$) plasma concentrations were more elevated in the DSSI group vs the other groups. Inverted circadian rhythm was associated with a higher expression of Per2 and a lower expression of epithelial Claudine-1 and TNF-$\alpha$ in inflamed colonic mucosa.
**Conclusion:** Disruption of circadian rhythm in mice is associated to a more severe colitis, characterized by a more severe systemic inflammation and higher concentrations of fecal calprotectin.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0252 THERAPEUTIC EFFECT OF GHRELIN IN ACETIC ACID-INDUCED COLITIS DEPENDS ON THE RELEASE OF ENDOGENOUS GROWTH HORMONE AND IGF-1

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**Introduction:** Inflammatory Bowel Disease (IBD) is a chronic relapsing inflammation of the digestive tract with alternative periods of exacerbation and remission. There are numerous methods to treat IBD, but medication that would ensure permanent therapeutic effect has not been found so far. Therefore, it is vital to search for the new therapeutic strategies. Ghrelin, an acylated 28-amino acid polypeptide, has been primarily shown to exhibit protective and therapeutic effect in the gut. Administration of ghrelin after induction of acute pancreatis accelerates pancreatic recovery in the course of this disease. In the stomach and duodenum, pretreatment with ghrelin reduces mucosal damage. Moreover, previous studies have suggested that ghrelin reduces colonic inflammation induced by trinitrobenzene sulfonic acid.
**Aims & Methods:** The aim of present studies was to assess the influence of ghrelin administration on the course of acetic acid-induced colitis. Moreover, we examined the role of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in ghrelin's effects in this inflammation. Materials & Methods: Studies have been performed on male Wistar rats. Before induction of colits animals were hypophysectomised or sham-operated. After two-week recovery, colitis was induced by a rectal enema of 1 ml of 3% solution of acetic acid. Saline or ghrelin (given at the dose of 8 nmol/kg/dose) were administered intraperitoneally twice a day and the first dose saline or ghrelin was given 24 h after rectal enema of acetic acid. Seven days after inductions of colitis, rats were anesthetized and colonic mucosal blood flow, and area of colonic mucosa damage were measured. Blood was taken for determination of serum concentration of GH and IGF-1. Biopsy samples of colonic mucosa were taken for biochemical examination.
**Results:** Rectal acetic acid enema induced colitis in all animals. Treatment with ghrelin for 6 days accelerated the healing of colonic mucosa. Ghrelin reduced damage of colonic wall and improved blood flow in colonic mucosa. This effect was associated with a significant reversion of the acetic acid-evoked decrease in mucosal DNA synthesis. Moreover, ghrelin administration reduced mucosal concentration of IL-1$\beta$ and activity of myeloperoxidase. Hypophysectomy increased the severity of mucosal damage and delayed the healing of the acetic acid-induced colitis. These effects were associated with additional reduction in mucosal blood follow and DNA synthesis. Mucosal concentration of IL-1$\beta$ and mucosal activity of myeloperoxidase were maximally increased. Administration of ghrelin was without any therapeutic effect in the course of the acetic acid-induced colitis in hypophysectomised rats. Treatment with ghrelin increased serum level of growth hormone and IGF-1 in pituitary-intact rats. Hypophysectomy lowered serum concentration of GH under the detection limit and reduced serum level of IGF-1 by about 90%. Administration of ghrelin failed to affect serum level of GH and IGF-1 in hypophysectomised rats.
**Conclusion:** Administration of ghrelin accelerates the healing of the acetic acid-induced colitis. Therapeutic effect of ghrelin in experimental colitis is mediated by the release of endogenous growth hormone and IGF-1.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0253 IONIZING DIAGNOSTIC RADIATION EXPOSURE IN PATIENTS WITH CROHŃS DISEASE: A RETROSPECTIVE STUDY IN A MEDIUM HOSPITAL AND ITS PREDICTIVE FACTORS

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**Introduction:** It is estimated that diagnostic medical radiation exposure may be responsible for up to 2% of cancers worldwide. Because of the relapsing course of Crohn's disease (CD), these patients usually require multiple ionizing radiation tests. The cumulative effective dose (CED) >50mSv is associated with an increased risk of developing certain solid tumours.
**Aims & Methods:** Our aim was to estimate the total CED and the CED due to the disease (CEDD) and to identify the risk factors associated with the exposure to a CEDD >50mSv. Design: retrospective cohort study (2001-20014). Population: patients with CD. Analysed variables: age, gender, disease duration, Montreal classification (age of onset, behaviour, location, perianal disease), history of major surgery, treatments and severity (major surgery and/or immunomodulator treatment and/or biological therapy), radiological tests, total CED and CEDD. Statistical analysis: for identifying predictive factors for receiving a CEDD

> 50mSV, an univariate and a multivariate analyses were performed using a > 50mSv dose as dependent variable.
**Results:** 297 CD patients were included, with a median disease duration time of 7 years (IQR = 4-14). 73.1% met severity criteria. The median total CED was 20.8 mSV (IQR = 5.9–48.3), being 24.6% > 50msV. The median CEDD was 10mSv (IQR = 3-31), being a 15.2% of patients > 50mSv. The more common tests were abdominal x-ray (63%), small bowel follow-through (58.95%) and abdominal computed tomography (47.9%). Patients receiving more radiation: women (median 13mSv (IQR 3-31.5)), >40 years old (median 13 mSv (IQR 3-35.3)), B2 (median 23.5mSv (IQR 5.2-53.3)) and B3 (median 40mSv (IQR 3-70)), L1 (median 20mSv (IQR 3-43), severity (median 20mSv (IQR 3-43)), major surgery (median 29.5mSv (IQR 3-56.8)), inmunomodulator (median 20msV (IQR 3-43)) and biological therapies (median 23 mSv (IQR 3-50)). Variables associated with a CEDD > 50mSv: inflammatory versus stricturing/penetrating (OR = 10.5; $IC_{95\%}$ (4.7–23.6); $p < 0.001$), major surgery (OR = 4.19; $IC_{95\%}$ (2.2–8.1); $p < 0.001$), inmunomodulator (OR = 4.5; $IC_{95\%}$ (1.7–11.9); $p < 0.001$) and biological treatments (OR = 3.6; $IC_{95\%}$ (1.9–6.9); $p < 0.001$) and severity (OR = 20.1; $IC_{95\%}$ 2.7–148.4); $p < 0.001$). In the multivariate analysis, the following variables were identified as independent predictors associated with an CEDD > 50mSv: major surgery (OR = 2.1; $IC_{95\%}$ (1.1–3.8); p = 0.019) and severity (OR = 20.6; $IC_{95\%}$ (4.5–94.8); $p < 0.01$).
**Conclusion:** Around a quarter of our patients with CD have received dangerous radiation. The severity of the disease and major surgery are predictive factors for receiving a CEDD > 50mSV. Monitoring patients' CED could be useful to reduce the exposure to potentially carcinogenic ionizing radiation. Alternative imaging tests not using ionizing radiation such as ultrasounds and abdominal magnetic resonance enterography should be considered in CD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0254 CLAUSII IN COLITIS: ROLE AND MECHANISMS OF ACTION OF BACILLUS CLAUSII IN EXPERIMENTAL COLITIS

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**Introduction:** *Bacillus clausii* is a gram-positive bacteria, used as in spore form as a probiotic. It is wide use in acute diarrhea, little is known about its ability to modify intestinal microbiota.
**Aims & Methods:** Aim of this study is to investigate the effect of *B. clausii* on mice acute DSS colitis, experimental condition mimicking human IBD and we evaluated gut microbiota modulation in this animal models. Mice were exposed to 2.5% of DSS for 5 days, with or without concomitant administration of *B. clausii* by oral gavage at two different doses. Stool samples were cultured for microbiological analysis before starting the experiments (day 0), at the end of the DSS treatment: 5 days and 14 days. Every other day, disease activity index was calculated based on body weight monitoring, fecal occult blood and type of feces. At sacrifice, histology was analyzed. The direct microbial properties of *B. clausii* were also evaluated in vitro using aerobic and anaerobic selective culture media.
**Results:** Higher dose of *B. clausii* (80 millions) significantly ameliorated mild DSS colitis in mice, according to DAI. No major changes were found on body weight in treated and untreated mice. Histology showed a lower inflammatory score for mice treated with *B. clausii* lower dose and a reduction of inflammatory total score. *B. clausii* modulates gut microbiota composition in mild DSS murine colitis in stool samples in colitic mice: colitic mice displayed lower counts of aerobic bacteria and higher anaerobes in fecal samples compared to healthy mice. The treatment with *B. clausii* associated to an increased counts of aerobes, in a dose dependent fashion. No major change were observed in anaerobic bacteria, treated or not with *B. clausii*. Finally, when used in vegetative form, *B. clausii* reduced the total count of *P. aeruginosa* in aerobic conditions, when compared to control.
**Conclusion:** As we obtained unexpected positive modulatory properties of *B. clausii* on murine colitis, in accordance with the medical advice and we concentrated on characterization of microbiota within fecal compartment of treated mice. We evaluated a histological characterization of the colonic inflammatory infiltrate within intestinal mucosa. The treatment with *B. clausii* was associated to a measurable effect on gut microbiota composition, resulting, in particular, in a reduction of *Staphilococcus aureus*, *Clostridium innocuum* and *Enterobacteriacae* like *Klebsiella oxytoca*, *Enterococcus casseliflavus* and *gallinarum*. *B. clausii* improves acute mild colitis in mice while in-vivo modulating gut microbiota by increasing total counts of aerobics.
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All other authors have declared no conflicts of interest.

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## P0255 IBD PHENOTYPES DIFFER IN GUT MYCOBIOTA COMPOSITION

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**Introduction:** Inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), is chronic idiopathic disorder of gastrointestinal tract. Although its pathogenesis is not completely understood, the inflammation in IBD is a result of an aberrant immune response to commensal microbiota in genetically susceptible individuals. Since there is a marked association of CD with gut fungal microbiota (mycobiota) we analyzed its composition in patients with CD, UC and in healthy controls.
**Aims & Methods:** We obtained stool samples from 9 CD patients, 7 UC patients and 3 healthy controls and extracted DNA using repeated bead–beating technique. Next, we analyzed mycobiota composition by sequencing internal transcribed spacer (ITS2) region of fungal DNA using Illumina MiSeq. The data were processed using standard Qiime pipeline, and the mycobiome alpha (Simpson's evenness index) and beta diversity (binary Jaccard metrics) were calculated.
**Results:** Number of detected fungal OTUs was not significantly different among groups healthy = 4.7 ± 0.6, CD = 5.9 ± 3.1 and UC = 7.6 ± 2.5). Either form of IBD clearly increased mycobiome variability, as documented by an increase in alpha diversity in CD and UC. All healthy individuals have similar fungal communities, dominated by well-adapted natural symbionts such as orders Saccharomycetales and Onygenales. In IBD, these communities were disrupted, and several other fungi were acquired from the environment. These major qualitative differences are well documented by tight clustering pattern of all three groups, as measured by binary Jaccard metrics. This was caused mainly by appearance of Davidiellaceae family and decrease in diversity within order Saccharomycetales in IBD patients.
**Conclusion:** These preliminary data show that gut mycobiota has significant pattern associated with health and disease. The high variability and presence of acquired fungi suggest that disrupted gut microbial ecology in IBD support transient fungal communities. Larger groups and more experiments are needed to confirm these interesting findings and to assess their medical relevance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0256 HIGHER DISEASE ACTIVITY IN ULCERATIVE COLITIS PATIENTS WITH ESBL PRODUCING ENTEROBACTERIACEAE GUT COLONIZATION: PRELIMINARY STUDY RESULTS

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**Introduction:** Extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae are the most frequently found multi-drug resistant bacteria colonizing the gut of ulcerative colitis (UC) patients. Changes in the microbiome may act as a trigger in UC inflammatory process. The objective of this study was to analyze whether the gut colonization with ESBL producing Enterobacteriaceae is associated with clinically relevant disease activity increase according to Mayo score, Montreal classification, Truelove and Witt's index.
**Aims & Methods:** All consecutive patients with histologically confirmed UC, hospitalized in Riga East Clinical University Hospital 2012 – 2015 were interviewed, rectal swabs were collected, Enterobacteriaceae were cultured and analyzed for ESBL presence according to EUCAST guidelines. Patient disease activity was evaluated according to Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part 1, that recommended clinically used severity indexes: Mayo score, Montreal classification, Truelove and Witt's index.
**Results:** A total of 65 patients with ulcerative colitis were tested for gut colonization with ESBL producing Enterobacteriaceae. We found that 7 (10.8%) of the ulcerative colitis patients were colonized with ESBL producing Enterobacteriaceae. Mean disease activity according to Mayo score in patients without ESBL producing Enterobacteriaceae colonization was 3.40 (SD = 1.98),

whereas in patients with ESBL producing Enterobacteriaceae colonization it was 5.86 (SD = 3.24) (n = 0.015). Most of the patients without ESBL producing Enterobacteriaceae colonization (n = 37; 63.8%) were in clinical remission, whereas most of the patients with ESBL producing Enterobacteriaceae colonization (n = 4; 57.1%) had moderate disease activity, according to Montreal classification disease severity section (p = 0.031). Most of the patients without ESBL producing Enterobacteriaceae colonization (n = 52; 89.7%) had mild disease activity, whereas most of the patients with ESBL producing Enterobacteriaceae colonization (n = 4; 57.1%) had moderate disease activity, according to Truelove and Witt's index (p = 0.008).

**Conclusion:** Higher disease activity is found in ulcerative colitis patients with ESBL producing Enterobacteriaceae gut colonization, according to three most frequently used UC disease activity scores – Mayo score, Montreal classification and Truelove and Witt's index. Such finding could be clinically relevant, because eradication of ESBL producing bacteria might reduce UC disease activity.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0257 THE PROTECTIVE EFFECT OF METFORMIN ON MATAINING INTESTINAL BARRIER FUNCTION IN COLITIS

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**Introduction:** The intestinal epithelium serves as an important barrier to prevent intestinal penetration of liminal bacteria, toxins and antigens. The integrity of intestinal epithelial barrier is disrupted in IBD patients. Metformin, which is used in the treatment of type 2 diabetes, was show to have additional benificial effects including anti-inflammation, anti-tumor, improvement of lifespan, modulation of gut microbiota. In the current study, we explore whether metformin could matain the intestinal epithelial function in DSS-induced colitis.

**Aims & Methods:** C57BL/6 mice were given ad libitum access to 3% DSS dissolved in the drinking water 7 days to induced acute colitis. The colitis mice were gavaged with metformin (100 mg/kg/day and500mg/kg/day) or PBS daily since colitis induction. The disease activity index (DAI) was assessed daily. The severity of inflammation was assessed by histopathological analysis. The inflammatory factors IL-6, TNF-$\alpha$and IL-1$\beta$were tested by real-time PCR and Elisa. The mRNA level of tight junction proteins zo-1, occludin and Muc 2 were determined by real-time PCR. Western blot was used to test the level of zo-1 and occludin in colon. To determin the bacterial translocation, the total population of bacteria in the MLNs, liver and spleen of colitis mice were assessed by qPCR.

**Results:** Metformin can significancantly ameliorate the induction of colitis by DSS, prevnets the reduction of body weight and colon length and reduces DAI score. Metformin significancantly inhibits the production of inflammatory factors IL-6, TNF-$\alpha$and IL-1$\beta$in DSS-induced colitis. Metformin treatment reuduces the loss of globet cell in colon of colitis mice. Compared to the DSS group, the level of zo-1, occludin and Muc2 are greatly higher after metformin administration. In addition, metformin can alleviate bacterial translocation caused by DSS-induced colitis.

**Conclusion:** Metfomin can ameliorate the severity of DSS-induced colitis through the potential mechanism involving its effects on mataining intestinal barrier function.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0258 FAMILIAL AGGREGATION OF INFLAMMATORY BOWEL DISEASE ON THE FAROE ISLANDS – A FAROESE IBD COHORT STUDY

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**Introduction:** Over the last two decades the incidence of inflammatory bowel disease (IBD) has increased dramatically on the Faroe Islands[1]- an archipelago located in the North Atlantic Ocean populated by an endogamous population - and is today the highest in the world[2]. This steep increase in IBD is mainly caused by ulcerative colitis (UC), since the incidence of Crohn's disease (CD) has remained stable over the last 5 decades. The reasons for these observations are unknown.

**Aims & Methods:** In this study we aimed to investigate the genetic contribution component in CD and UC patients on the Faroe Islands. The Faroese IBD cohort is a population-based, nationwide cohort of all patients diagnosed with Crohn's disease (CD), ulcerative colitis (UC), and IBD unclassified (IBDU) according to the Copenhagen diagnostic criteria from 1960 until 2014. The relationship among CD and UC patients was studied using a unique computerized nationwide genealogy registry covering pedigrees from the whole Faroese population from approx. 1650. Relative risk (RR) of kinship for patients were compared to controls (simulated as if they were probands and shown as CI93%). Controls were matched for age, gender and approximate sibship size. Pedigrees for control subjects were randomly and reiteratively sampled from the Faroese genealogic database.

**Results:** Pedigrees were available for the whole cohort consisting of 664 incident IBD patients, 113 (17%) with CD, 417 (62%) with UC, and 134 (21%) with IBDU diagnosed according to the Copenhagen Diagnostic Criteria for IBD. Average age at diagnosis was 41 years (0–86 yrs). Disease extent for UC patients at diagnosis was proctitis in 21%, left-sided colitis in 39%, and extensive colitis in 40%. For CD patients the disease behavior was nonstricturing/nonpenetrating (B1) in 65%, stricturing (B2) in 25%, and penetrating (B3) in 8% at the time of diagnosis. Only 2% of CD patients had perianal disease. Disease location for CD patients as terminal ileum (L1) in 22%, colon (L2) in 65%, ileo-colon (L3) in 10%, and upper GI (L4 (+/- L1-L3) in 3%. The RR of kinship in UC and CD patients compared to controls are shown in table 2. Overall, UC patients were more closely related than controls (RR for UC was higher than upper CI93% limit for controls), whereas no hereditary component in CD patients was found.

**Conclusion:** In this population-based, nationwide cohort of Faroese IBD patients a hereditary component was found for UC but not for CD patients. Further analyses on the impact of the genetic contribution on disease course as well as genetic and microbial analysis are ongoing.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0259 MEDICAL THERAPY, SURGERY AND HOSPITALIZATION RATES DURING THE 2-AND 3-YEAR FOLLOW-UP OF THE 2011 ECCO-EPICOM COHORT

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**Abstract No: P0258**

**Table 1:** Relative risks of kinship for IBD patients and controls.

| Family relation | Ulcerative colitis Relative risk | Controls – ulcerative colitis (RR CI93%) | x times higher risk for UC vs upper bound in controls | Crohn's disease Relative risk | Controls – Crohn's disease (RR CI93%) | x times higher risk for CD vs upper bound in controls |
|---|---|---|---|---|---|---|
| **1st degree relatives** | | | | | | |
| Sibling | 2.74 | 1.46-2.08 | 1.3 | 0.99 | 0.00–0.57 | 1.7 |
| Child | 2.09 | 0.81–1.88 | 1.1 | 0.46 | 0.00–0.46 | 1.0 |
| **2nd degree relatives** | | | | | | |
| Uncle/Aunt | 1.44 | 0.72–0.79 | 1.8 | 0.09 | 0.00–0.28 | 0.3 |
| Niece/Nephew | 1.27 | 0.98–1.14 | 1.1 | 0.12 | 0.00–0.42 | 0.3 |
| Grandchild | 0.99 | 0.20–0.79 | 1.3 | 0.55 | 0.00–0.00 | 0.0 |
| **3rd degree relatives** | | | | | | |
| First cousins | 0.90 | 0.94–1.18 | 0.8 | 0.07 | 0.22–0.52 | 0.1 |

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**Introduction:** The ECCO-EpiCom study investigates the differences in the incidence, disease characteristics and therapeutic strategy of inflammatory bowel diseases (IBD) between Eastern and Western Europe.

**Aims & Methods:** Our aim was to analyze differences in the 2-and 3-year outcomes between Eastern Europe and Western Europe/Australia in the 2011 ECCO-EpiCom cohort. Eight Western European, 5 Eastern European and one Australian center participated in the 2-and 3-year follow-up. Patients' data on medical therapy, surgery and hospitalizations were registered in the web-based ECCO-EpiCom database.

**Results:** 319 IBD patients (Crohn's disease (CD): 126, (ulcerative colitis (UC): 160, IBD unclassified: 33; 234 patients from Western Europe/Australia and 85 patients from Eastern Europe; median age at diagnosis: 38.2 years (range: 15.1–88.6); F/M: 137/182) have completed the 2-year and 269 IBD patients completed the 3-year follow-up. During the 2- and 3-year follow-up period, 24 (67%) and 24 (75%) CD patients from Eastern Europe and 54 (60%) and 56 (68%) from Western Europe/Australia received IS (immunosuppressives) ($p = NS$). Five (14%) and 5 (16%) CD patients from Eastern Europe and 27 (30%) and 29 (35%) from Western Europe/Australia received biological therapy ($p_{2\text{-year}} = 0.06$ and $p_{3\text{-year}} = 0.04$). Nine (25%) and 9 (28%) CD patients from Eastern Europe and 9 (10%) and 9 (11%) CD patients from Western Europe/Australia underwent surgery ($p_{2\text{-year}} = 0.03$ and $p_{3\text{-year}} = 0.02$). Twelve (33%) and 12 (38%) CD patients from Eastern Europe and 26 (29%) and 28 (34%) from Western Europe/Australia were hospitalized ($p_{2\text{-year}} = 0.62$ and $p_{3\text{-year}} = 0.70$). During the 2- and 3-year follow-up period, about a third of the UC patients received IS in both Eastern Europe and Western Europe/Australia 3-year follow-up: Eastern Europe: 12 (39%) Western Europe/Australia: 33 (34%) $p = NS$. No difference was found in biological use, surgery and hospitalization rates in UC patients both during the 2-and 3-year follow-up period (biological therapy: 3-year follow-up: Eastern Europe: 4 (13%), Western Europe/Australia: 15 (16%) $p = 0.72$; colectomy: 3-year follow-up: Eastern Europe: 1 (3%) Western Europe/Australia: 5 (5%) $p = 0.66$; hospitalization: 3-year follow-up: Eastern Europe: 9 (29%) Western Europe/Australia: 33 (34%) $p = NS$).

**Conclusion:** At 2 and 3 years after diagnosis, the biological use in CD patients was higher in Western Europe/Australian centers compared to Eastern Europe. The surgery rate was lower in the former, while IS use and hospitalization rates were not different. In UC, IS and biological use, colectomy and hospitalization rates remained similar between these regions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0260 REAL-WORLD EPIDEMIOLOGY AND INITIAL TREATMENT PATTERNS OF PATIENTS NEWLY DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE IN ISRAEL

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**Introduction:** To describe the real-world epidemiology and treatment patterns of patients newly diagnosed with inflammatory bowel disease (IBD) in Israel, including ulcerative colitis (UC) and Crohn's disease (CD).

**Aims & Methods:** A retrospective cohort study was performed using the computerized databases of Maccabi Healthcare Services, a 2-million-member healthcare maintenance organization with similar demographic characteristics to the general population in Israel (representing 25% of the Israeli population), in a context of universal and mandatory health insurance. Patients newly diagnosed with IBD in 2010–2014 were defined by at least 2 separate diagnoses (including one from a gastroenterologist or hospital) and 12 months of enrolment prior to their first diagnosis. For the analysis of treatment patterns, patients were required to have purchased a disease-related pharmacotherapy on/after IBD diagnosis (index purchase) and have 12 months of follow up through 2015. Patients were classified by index therapy based on the first purchase after diagnosis. Excluded were patients who initiated biologics prior to IBD diagnosis. In order to group patients by unique index therapy class, 25 patients with a combined index purchase of immunomodulators (IMs) and 5- aminosalicylates (5-ASA) were also excluded. Changes from index therapy in the first 12 months were described, including discontinuation (based on an observed treatment gap $\geq$ 60 days), switching, add-on therapy and upward dose titration, assuming an induction or dose-adjustment period of 90 days for 5-ASA, IM and biologics.

**Results:** During 2010–2014, the incidence rates for newly diagnosed UC ($N = 1$, 120) and CD ($N = 1$, 704) were 11.4 and 17.3 per 100, 000 Maccabi Health Services members, respectively. A total of 1, 034 UC patients (mean age: $37.2 \pm SD$ 16.5 years) and 1, 251 CD patients ($33.0 \pm 16.9$ years) were included in the analyses of treatment patterns. In the year prior to index purchase, 179 patients (4.3% of UC and 10.8% of CD patients) had seen a gastroenterologist at least 5 times. 5-ASAs were the predominant index therapy during the study period, accounting for 90.2% and 66.4% of UC and CD patients, respectively. IMs were more frequently initiated among patients newly diagnosed with CD compared to UC (14.7% vs. 0.7%). Among 5-ASA initiators, almost half discontinued during the induction period. Add-on therapy consisted primarily of 5-ASA or CS for UC patients and of IM for CD patients. Among IM-initiating CD patients ($N = 184$), 8.7% switched directly to biological therapies within a year, accounting for the majority of switches in this sub-group. Overall, 86% and 9% of IBD patients used 5-ASAs and biologics, respectively, either at index or over the following 12 months.

**Conclusion:** Overall during the study period, high treatment uptake was observed among patients with newly diagnosed IBD, particularly with 5-ASAs and IMs. However, changes from index therapy or discontinuation were frequent within the first year, underscoring the complexity of initial treatment pathways among different patient sub-groups.

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G. Chodick: GC is an employee of Maccabi Health Services Israel and conducted the study with funding from Takeda Pharmaceuticals.
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J.M. Khalid: JMK is an employee of Takeda Development Centre Europe.
V. Shalev: VS is an employee of Maccabi Health Services Israel and conducted the study with funding from Takeda Pharmaceuticals.

## P0261 LONG-TERM OUTCOMES AND PREDICTORS OF DISABLING DISEASE AND BOWEL DAMAGE OF A POPULATION-BASED COHORT OF INCIDENT CROHN'S DISEASE DIAGNOSED BETWEEN 1995 AND 1997

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**Introduction:** At the era of early combined immunosuppressive treatment, identification of early prognostic factors of a complicated or disabling Crohn's disease course is needed for physician decision-making to minimize structural bowel damage, complications of disease and side effects related to treatment. Only population-based studies are able to assess these questions given the selection bias of referral center studies.

**Aims & Methods:** All incident cases of patients diagnosed with possible CD ($n = 370$) were registered from 1994 to 1997 in Brittany, a limited area in France. At diagnosis were recorded clinical features, endoscopic lesion per ileocolic segment (according to the CDEIS), radiologic and histologic data. All charts of patients were reviewed from the diagnosis to the last clinic in 2015. Disabling Crohn's disease course was defined according to the Saint-Antoine criteria: more than 2 steroid course or steroid dependency/resistance, hospitalization related to CD, use of immunosuppressant or anti-TNF, anal or major abdominal surgery. Bowel damage was defined according to the criteria that weight the recent Lémann Score (surgery, complicated behavior, anoperineal involvement) Independent predictors of all outcomes were identified using a Cox proportional hazards model.

**Results:** Among the 370 incident cases, 39 had not Crohn's disease and 272 of the 331 cases with CD (82%) were reviewed with a median follow-up of 12.8 years. Disease locations were broadly similar for each patient over time involving the ileon for 15% of patient, the colon for 36% of patient and ileocolic for 48% of patients. Cumulative probabilities of stricturing disease and fistulizing disease at 15 years were 35% 95%IC [29%–42%] and 17% 95%IC [12%–22%], respectively. Cumulative probabilities of complicated behavior (structuring or fistulizing disease) were at 5 years, 10 years, and 15 years, 23%, 34% and 42%, respectively. Cumulative probabilities of major abdominal surgery were at 1 year, 5 years, 10 years and 15 years, 14% [10%–19%], 29% [24%–35%], 36% [30%–42%] and 45% [38%–52%], respectively. The cumulative probabilities of the use of steroids, immunosuppressant (thiopurine and methotrexate) and TNF antagonist were 65.8% ($n = 179$), 37.5% ($n = 102$) and 22.1% ($n = 60$) at 15 years. Median disease duration before the use of immunosuppressant or TNF antagonist were 68 months and 131 months, respectively. Cumulative probabilities of disabling disease were at 1 year, 5 years, 10 years and 15 years, 35% [29%–41%], 57% [50%–63%], 67% [61%–73%] and 74% [68%–79%], respectively. Systemic manifestation at diagnosis ($HR = 1.62$ [1.09–2.39], $p = 0.02$) and perianal lesion ($HR = 4.47$ [1.80–11.08], $p = 0.001$) independently predicted a disabling disaese course. Endoscopic lesions at diagnosis were not associated with disease outcomes. Bowel damage was observed for 154 patients after

mean disease duration of 15 months. The cumulative probabilities of having bowel damage were 14%, 34%, 44% et 51%, at 1 year, 5 years, 10 years et 15 years, respectively. L1 disease (HR = 1.9, IC95 [1.2–2.9]), diagnostic delay of at least 9 months (HR = 1.7, IC95 [1.17–2.4]) and extraintestinal manifestation (HR = 1.44, IC95 [1.01–2.03]) predicted at diagnosis bowel damage in the long term.

**Conclusion:** In a population-based cohort, most patients experienced disabling disease outcomes according to the predefined Saint-Antoine criteria. Half of patients had bowel damage that occurred early in the course of CD. The high rate of disabling outcomes may underline the need to treat CD patients with effective treatment whatever the disease characteristics at diagnosis, including endoscopic lesions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0262 IS CELIAC DISEASE AN UNRECOGNIZED RISK FACTOR FOR INFLAMMATORY BOWEL DISEASE?

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**Introduction:** There appears to be an association between inflammatory bowel disease (IBD) and Celiac Disease (CeD). The aim of this systematic review was to assess in IBD patients the risk of CeD and in CeD the risk of IBD.

**Aims & Methods:** With the search term 'inflammatory bowel disease' & 'celiac disease', 28 studies (17 IBD in CeD, 13 CeD in IBD and 4 both) met inclusion criteria. Proportions and 95% Confidence Intervals (CI) for the prevalence of IBD in CeD patients and vice versa were compared with published prevalence rates for the respective geographic regions.

**Results:** Seventeen studies included 41, 482 adult IBD patients (20, 357 Crohn's disease (CD), 19, 797 ulcerative colitis (UC)), 459 patients with CeD. Overall, in IBD patients the prevalence of celiac disease was 1.065% (95% CI 1.065–1.2065) while the prevalence in CD and UC was 1.1888 (95% CI 1.0388–1.2288) and 1.0307 (95% CI 0.86307–1.1707). The prevalence of IBD in celiac disease was 1.6619 (95% CI 1.19–2.15). The prevalence for IBD in the respective geographic regions was 307 per 100.000 (95% CI). The expected adjusted prevalence of celiac disease in the study population was 1%. Thus our results show a 5.5 fold increase of IBD in CeD compared to the general population (6.6 fold for CD and 4.9 fold for UC).

**Conclusion:** The prevalence of IBD in CeD is increased, while the prevalence of CeD in IBD is not different from the expected prevalence in the various populations. Celiac disease is a risk factor for IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0263 OBJECTIVE ASSESSMENT OF PHYSICIAN TO PATIENT CONCORDANCE AND BIOPSYCHOSOCIAL IMPACT ON PERTINENT PATIENT REPORTED OUTCOMES AND MEDICATION COMPLIANCE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Enhanced attention to patient report outcomes (PRO) and medication compliance are associated with improved holistic care of inflammatory bowel disease (IBD) patients. This study aims to evaluate physician and patient concordance on PRO and compliance as well as the potential relationship with underlying biopsychosocial factors.

**Aims & Methods:** We conducted a prospective study on patients diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) presenting for evaluation at the McGill IBD center between September 2015 and March 2016. Patients were assessed for quality of life, disability and productivity using validated short IBD questionnaire (SIBDQ), IBD disability index (IBDDI) and work productivity assessment index (WPAI) respectively. Medication compliance was evaluated using the medication adherence questionnaire (MAQ) and selected psychological assessment was also performed using hospital anxiety and depression score (HADS) as well as brief COPE questionnaire for disease coping strategies. Disease activity was objectively determined by fecal calprotectin (FCP). Results were examined against the treating IBD physician's assessment on these measures, which was independently obtained using visual analogue following concurrent clinic review.

**Results:** 132 (91 CD / 41 UC) patients, with median age of 39 and 40% male, were included. The validated PRO evaluation tools correlated well with each other, despite their assessment on different outcomes (Pearson correlation coefficient r = 0.66–0.81), as well as with HADS (r = 0.62); $p < 0.001$ for all. Unexpectedly there was a strong concordance between physician perception and PRO measures of disability (r = 0.65), quality of life (r = 0.65) and productivity (r = 0.61) as well as disease activity (FCP: r = 0.64), $p < 0.001$ for all. Men were more likely to report worse disability (odd ratio [OR] 3.01, 95% confidence interval [CI] (1.21–7.49), p = 0.018) and quality of life (OR 5.63, 95% CI 2.02–15.72, p = 0.001). Disease activity (FCP > 250), high HADS and patient coping strategies did not reliably predict worse PRO on regression analysis. Medication compliance rate is poor in the study population (17% strong adherence rate) and it is inadequately identified by treating physicians (r = 0.20). Furthermore, in those asymptomatic patients (HBI ≤ 4 / partial Mayo ≤ 1) with higher risk of relapse as indicated by elevated FCP > 250, up to 43% report suboptimal compliance. Strong compliance (MAQ < 3) is independently predicted by active disease with FCP > 250 (OR 3.64, 95% CI 1.09–12.17, p = 0.036), age less than 30 (OR 3.57, 95% CI 1.53–8.34, p = 0.003) and poor quality of life (SIBDQ < 47: OR 2.70, 95% CI 1.18–6.21, p = 0.019) on univariate analysis. FCP > 250 is the only factor independently associated with compliance on multivariate analysis (OR 6.41, 95% CI 1.46–28.18, p = 0.014).

**Conclusion:** Pertinent patient-reported outcomes of disability, quality of life and productivity can be accurately and effectively identified by treating physicians in standard clinical settings without the necessary need of administering extensive qualitative questionnaires. Strong medication compliance is associated with disease activity however more emphasis needs to be made on addressing adherence issues, particularly in those with high risk of risk relapse.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0264 THE ONLINE HEALTH CARE REVOLUTION AND THE ASSOCIATION BETWEEN UNCERTAINTY AND QUALITY OF LIFE IN CROHN'S DISEASE

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**Introduction:** The internet has revolutionized our daily life. Recent studies found that medical-related searches ranked third as one of the most frequent online activities.

Individuals seek information in order to understand symptoms, treatment, options, and prognosis but the benefits haven't come without consequences.

**Aims & Methods:** To examine the association between seeking health information via internet and health related quality of life (HRQOL) and uncertainty among Crohn's disease (CD) patients.

Methods: The research tool was composed of a 4 parts questionnaire; demographic and clinical information; HRQOL (The short inflammatory bowel disease questionnaire), level of certainty (the Mishel Uncertainty in Illness Scale), and information gathered via internet regarding CD questionnaire.

**Results:** 105 consecutive patients participated in the study, mean age was 34.2 ± 10.7 years. Sixty-three percent of participants reported of seeking information via internet about their disease during the last 3 months. The results show a positive significant correlation between HRQOL and certainty (P = 0.002) and a negative correlation between certainty and seeking information via internet (r = −0.19, p = 0.05). Multiple regression analysis for factors associated with HRQOL, found level of certainty, seeking information via internet, and disease activity significant factors for quality of life. Seeking information via internet was significantly associated with level of certainty.

**Conclusion:** This is the first study examined the relationship between seeking information via internet, HRQOL and level of certainty in patients with CD. Understanding factors affecting level of certainty and HRQOL can provide tools for caregivers for better treatment of CD patients, focusing on dedicated web information.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0265 ASSOCIATION BETWEEN POUCHITIS AND MICRORNA EXPRESSION AFTER RESTORATIVE PROCTOCOLECTOMY IN PATIENTS WITH ULCERATIVE COLITIS

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**Introduction:** Restorative proctocolectomy with ileal pouch-anal anastomosis is the standard surgical procedure for patients with ulcerative colitis (UC). Pouchitis, a non-specific inflammation of the ileal reservoir, is the most common long-term complication. MicroRNAs (miRNAs) are small, noncoding RNAs that act as potent negative regulators of gene expression and are differentially expressed in chronic inflammatory diseases, including UC. To our knowledge, little is known about the relationship between pouchitis and miRNA expression. This study was aimed to determine whether miRNA expression is altered in pouchitis.

**Aims & Methods:** Sixty-four patients were included in this study. Modified Pouch Disease Activity Index (mPDAI) was used for the diagnosis of pouchitis; an mPDAI of no less than four was indicative of pouchitis. We identified 16 pouchitis patients, and the rest were considered non-pouchitis patients. Biopsies were

obtained by pouch endoscopy, and the total RNA was extracted, reverse-transcribed, and quantified with real-time polymerase chain reaction. The relative quantification (RQ) value was calculated according to the manufacturer's instructions. Statistical analyses for qRT-PCR were performed using non-parametric Mann-Whitney test. Statistical significance was set at $p < 0.05$.
**Results:** We compared miRNA expression between samples from pouchitis and those from non-pouchitis. We have demonstrated that two miRNAs (miR-21, miR-223) increased (RQ = 1.352 (1.125–1.625), p = 0.004; and RQ = 1.371 (1.039–1.809), p = 0.014, respectively) and two miRNAs (miR-192, miR-196a) decreased (RQ = 0.611 (0.381–0.979), P = 0.036, RQ = 0.716 (0.541–0.958), p = 0.019, respectively) in the inflamed mucosa of pouchitis compared with the control. Next, we compared miRNA expression between samples from pouchitis and those from the proximal non-inflamed ileum. We found that fourteen miRNAs decreased in the inflamed mucosa of pouchitis compared with that in the proximal region without inflammation (Table). Two miRNAs (miR-192, miR-196a,) were downregulated analogously in pouchitis samples compared with samples from non-pouchitis and those from the proximal samples.

Comparison in miRNA expression between pouchitis and the proximal ileum

| MiRNA | Relative quantification | P value |
|---|---|---|
| miR-7 | 0.69 (0.54–0.89) | 0.008 |
| miR-16 | 0.79 (0.66–0.94) | 0.049 |
| miR-17 | 0.72 (0.57–0.93) | 0.045 |
| miR-29c | 0.73 (0.61–0.88) | 0.006 |
| miR-106a | 0.69 (0.54–0.89) | 0.014 |
| miR-145 | 0.65 (0.46–0.91) | 0.042 |
| miR-188 | 0.67 (0.53–0.84) | 0.037 |
| miR-192 | 0.24 (0.15–0.39) | <0.001 |
| miR-195 | 0.76 (0.62–0.93) | 0.041 |
| miR-196a | 0.60 (0.45–0.80) | 0.006 |
| miR-200b | 0.45 (.32–0.65) | <0.001 |
| miR-221 | 0.58 (0.46–0.74) | <0.001 |
| miR-422a | 0.51 (0.38–0.68) | <0.001 |
| miR-499 | 0.69 (0.53–0.90) | 0.033 |

**Conclusion:** We found a statistically significant difference in miRNA expression in pouchitis tissues. MiRNA may play a significant role in the pathogenesis of pouchitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0266 VARIANTS OF IL23R GENE AND CROHN'S DISEASE

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**Introduction:** The pathogenesis of inflammatory bowel disease (IBD) is very complex. It is related to factors both genetic, immunological and environmental. Numerous studies have associated susceptibility genes to these diseases. Among the genes that have been recently implicated in IBD susceptibility we note the IL23R.
Its role in inflammation and in innate and adaptive immunity makes it a strong candidate involved in triggering certain autoimmune and inflammatory diseases. This locus includes many polymorphisms or SNPs including 11209026 SNP and the 7517847 SNP which are the interest of our study.
**Aims & Methods:** Our aim is to study the 11209026 SNP and the 7517847 SNP of the IL23R gene in our country's population in order to assess the involvement of these two variants in the susceptibility to Crohn's disease (CD). We began a preliminary study by seeking the presence of mutations for each SNPs of IL23R gene in the Tunisian population while relying on studies that concerned the two polymorphisms 11209026 and 7517847. Molecular analysis of IL23R gene was made on 28 patients with Crohn's disease and 37 healthy controls. We conducted a verification of the presence of the SNPs in the DNA sequences extracted from whole blood of patients and healthy controls. The extraction was made using two techniques: phenol / chloroform for healthy controls and by KIT Quiagen for patients with CD. Then, amplification of the 11209026 SNP and the 7517847 SNP is carried out using specific primers that amplify the exon 9 of IL23R gene for the first and intron 6 of the gene for the second one. The primers' design was done using a bioinformatic tool: Primer 3 software to amplify the region of interest. The primers designed to amplify the SNP 11209026 have a 298 bp band size and the SNP 7517847 provides an amplicon of 378 bp. The next step is to confirm that the amplification products correspond to the amplified regions and if they contain polymorphisms at their sequences. The technique used for this purpose is that of sequencing followed by statistical analysis of allele and genotype frequencies.
**Results:** PCR results confirmed the specificity of the primers since we obtained a 208 bp band for patients with CD. Similarly for the 2nd SNP, we had the expected band size of 378 bp for both patients and controls.
Analysis of the results showed for the SNP 11209026 the presence of the rare allelic polymorphism A in the nucleotide sequences of the DNA of patients with CD. Thus the frequency of this rare allele A is 0.08 which is close to the frequency found in other studies such as the population of Pennsylvania (1). The genotypic frequencies of the SNP12209026: GG (0.87) GA (11.9) and AA (0.8) are also acceptable on the basis of other studies that show quite similar values such as the population of New Zealand (2) and that of the German population (3). The absence of this allele in the SNP 112209026 sequence in certain populations is due to its rarity. As for the sequence analysis results for the second SNP 7517847 resulting in allelic and genotypic frequencies: It was shown that the G allele polymorphism or SNP G is found in the DNA sequence for both controls and CD patients. The frequency of the G allele was 0.17 for patients with Crohn's disease and 0.18 for healthy controls. These allele frequencies are also accepted by comparing the frequencies observed in the Polish population (4). Also, the genotypic frequencies of TT, TG and GG are present in our control population as observed in studies such as that of Rome and that of Hungary (5) with an allele and genotype frequencies close to those we found.
**Conclusion:** Our results show the presence of the rare allele A of the SNP11209026 (Arg 381Gln) in patients with CD and the G polymorphism of the 7517847 SNP in our country's population. Our study is the first studying our population by investigating a susceptibility gene as that of IL23R in CD. Further studies with largest numbers of patients are necessary to be able to study the implication of the presence of these polymorphisms on the presence and severity of CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0267 ASSOCIATION STUDY BETWEEN OCTN1 FUNCTIONAL HAPLOTYPES AND A PENETRATING BEHAVIOUR OF CROHN'S DISEASE IN A KOREAN POPULATION

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**Introduction:** In the pathogenesis of Crohn's diseases (CD) it is hypothesized that a dysregulated mucosal immune response to the intestinal environment in a genetically susceptible host. Organic cation/carnitine transporter 1 (OCTN1), one of CD associated genes, have been demonstrated that the non-synonymous variant p.L503F is associated with susceptibility to CD. However, it was reported that p.L503F is absent in Asian populations. Previously, we identified and functionally characterized that four genetic variants of the OCTN1 promoter region significantly changed a promoter activity in Koreans.
**Aims & Methods:** We examined whether four functional variants of the OCTN1 promoter play a role in the susceptibility to or clinical course of CD in Koreans. The frequencies of the four variants of the OCTN1 promoter were determined by genotyping using DNA samples from 194 patients with CD and 287 healthy controls. Then, association tests were performed between genetic variants and the susceptibility to CD or clinical course of CD.
**Results:** We identified that susceptibility to CD was not significantly associated with OCTN1 functional promoter variants or haplotypes showing altered promoter activities in in vitro assays. However, a penetrating behaviour in CD patients was significantly associated with OCTN1 functional promoter haplotypes showing decreased promoter activities (Hazards ratio = 2.428, P = 0.009).

**Table:** Clinical course of CD patients according to OCTN1 haplotypes.

| Parameter | Variant (%) | Control (%) | Hazards ratio (95% CI) | P value |
|---|---|---|---|---|
| Total number | 86 | 108 | | |
| Behavior | | | | |
| Inflammatory | 40 (46.5) | 68 (63.0) | | |
| Stricturing | 18 (20.9) | 27 (25.0) | 1.004 (0.549 – 1.837) | 0.990 |
| Penetrating | 28 (32.6) | 13 (12.0) | 2.428 (1.243 – 4.741) | 0.009 |
| Azathioprine or Anti-TNF agent use | 64 (74.4) | 81 (75.0) | 0.795 (0.566 – 1.115) | 0.184 |
| Surgery | 33 (38.4) | 32 (29.6) | 1.147 (0.702 – 1.875) | 0.584 |

**Conclusion:** Our results suggest that the OCTN1 functional promoter haplotypes can influence the penetrating behaviour of CD, although these might not be associated with susceptibility to CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0268 MRI REMISSION AFTER THERAPEUTIC INTERVENTION IS ASSOCIATED WITH MORE TIME SPENT IN CLINICAL CORTICOSTEROIDS-FREE REMISSION AND DECREASED RISK OF SURGERY IN CROHN'S DISEASE

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**Introduction:** To date, mucosal healing should be the therapeutic goal in Crohn's disease (CD) as it is associated with more favourable outcomes. However, repeating ileocolonoscopy to monitor the disease is felt as a burden by the patients and has led physicians to look for alternative noninvasive approaches. Thus, magnetic resonance imaging (MRI) has been increasingly used for the diagnosis and the monitoring of CD because of its lack of ionizing radiation, and its ability to accurately assess inflammation in CD. Recently, it has been shown that MRI is able to assess therapeutic efficacy [1]. However, whether achieving MRI remission is associated with favourable outcomes remains unknown.

**Aims & Methods:** We aimed to investigate whether MRI remission after therapeutic intervention could predict clinical corticosteroids-free remission (CFREM), hospitalization and CD related-surgery. We performed a posthoc analysis from pooled data of two prospective trials [2, 3]. Patients were excluded from this study if MRI examination was performed at diagnosis, if MRI was performed before starting/switching therapy, or if follow-up was shorter than 6 months. Objective sign of inflammation on colonoscopy, CTscan or MRI before treatment has to be available to include the patients in this study. Overall, 63 CD patients, undergoing MRI to monitor a therapeutic response, were included. All the patients underwent diffusion-weighted magnetic resonance enterocolonography with no bowel cleansing and no rectal enema. MRI evaluation was performed using 5 segments (ileum, right colon, transverse colon, left/sigmoid colon and rectum). MRI remission was defined using Clermont criteria [2, 3] (Clermont score dedicated to the ileum $< 18.9$ and no segmental apparent diffusion coefficient ADC $< 1.88$) or using Barcelona criteria [4] (no segmental MaRIA $> 11$). Deep MRI remission was defined as no segmental MaRIA $> 7$. Clinical corticosteroids-free remission was defined as absence of CD flare. CD flare was defined as reappearance or worsening of clinical manifestation leading to therapeutic modification, hospitalization or CD-related surgery. For each of the patients CFREM and hospitalization were assessed by semesters. Repeated data were analyzed using generalized linear mixed model (logistic) taking into account between and within patient variability as random-effect. Other data were analyzed with usual statistical tests.

**Results:** The characteristics of the 63 included patients were given in Table 1 with a median follow-up of 4 semesters.

Characteristics of the 63 Crohn's disease patients at inclusion (=time of MRI examination)

| Charateristics | Overall population (n = 63) |
|---|---|
| Female gender | 43 (68.3%) |
| Smokers | 32 (50.8%) |
| Age at diagnosis, years, (mean +/- sd) | 26.4 +/- 12.6 |
| Age at inclusion, years, (mean +/- sd) | 34.8+/- 14.5 |
| Disease duration, years, (mean +/- sd) | 8.7 +/- 9.5 |
| Montreal classification | |
| Location | |
| L1 | 19 (30.2%) |
| L2 | 18 (28.6%) |
| L3 | 26 (41.2%) |
| L4 | 6 (9.5%) |
| Behaviour | |
| B1 | 29 (46.0%) |
| B2 | 22 (34.9%) |
| B3 | 12 (19.0%) |
| Perianal lesions | 20 (31.7%) |
| Prior intestinal resection | 21 (33.3%) |
| CDAI, median [IQR] | 189[80-243] |
| CDAI > 150 | 39 (61.9%) |
| CRP, median [IQR] | 14.0[2.9-35.5] |
| CRP > 5 g/L | 37 (56.9%) |
| Current therapies at inclusion | |
| Corticosteroids | 25 (39.7%) |
| Thiopurines | 23 (36.5%) |
| Methotrexate | 1 (1.6%) |
| Anti-TNF | 30 (47.6%) |
| Infliximab | 12 (19.0%) |
| Adalimumab | 18 (28.6%) |
| MRI remission according Clermont criteria | 15 (23.8%) |
| MRI remission according Barcelona criteria | 14 (22.2%) |
| Deep MRI remission according Barcelona criteria | 11 (17.4%) |

Overall, 300 semesters were taken into account for the analysis. In multivariate analysis taken into account the impact of CDAI, CRP and current therapy at inclusion, deep MRI remission was associated with more time spent in CFREM (85.7% vs 44.9%, $p = 0.01$) and increased time to CD-related surgery ($p < 0.05$) compared to CD patients with persistent MRI activity. MRI remission according to Clermont criteria (67.1% vs 47.1%) and Barcelona criteria (66.7% vs 47.3%) ($p = 0.047$) were also associated with higher proportion of semester spent in CFREM. No definitions of MRI remission were associated with the percentage of semesters with hospitalization.

**Conclusion:** MRI remission after therapeutic intervention is associated with favourable outcomes and should be considered as non-invasive therapeutic endpoint in CD. A dedicated prospective trial should be led to confirm our data.

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All other authors have declared no conflicts of interest.

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## P0270 METABOLIC PROFILING OF URINE AND FAECES DIFFERENTIATES INFLAMMATORY BOWEL DISEASE PHENOTYPE AND HAS IMPLICATIONS ON THERAPEUTIC RESPONSE

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**Introduction:** Inflammatory bowel disease (IBD) is influenced by environmental and genetic factors which alter the gut microbiota. The human gut microbiota is involved in the maintenance of its host physiological functions and an imbalance in the microbial population with it's subsequent metabolic signatures may lead to disease activity and phenotypes.[1] Therapy with anti-TNF medication forms the backbone of treatment in moderate to severe Crohn's disease (CD) and is used as salvage therapy in severe acute ulcerative colitis (UC). The metabonomic approach using powerful analytical methods for metabolite detection have led to biomarker discovery and may help in differentiating IBD phenotypes and therapeutic response to medications.[2].

**Aims & Methods:** We aimed to investigate the variations occurring in polar metabolites via hydrophilic interaction liquid chromatography (HILIC) profiling between healthy, CD and ulcerative colitis cohorts in urine and faeces and response to anti-TNF therapy by profiling using a metabonomic approach. Urine and faeces were collected from 15 healthy controls, 58 patients with moderate to severe CD prior to commencement of anti- TNF and 8 patients with severe acute UC at the point of hospital admission. The samples were collected at three-monthly timepoints for 12 months at study exit or upon cessation of drug due to non-response or requirement for surgery. Metabolic profiling was performed on an Acquity UPLC system coupled to a Xevo G2 QTof mass spectrometer (Waters). Chromatography was performed using an Acquity BEH HILIC column (Waters). Separation was performed using gradient elution (20 min run) with 0.1% (v/v) formic acid and 10 mM ammonium acetate in 95/5% ACN/H2O

(A) and 0.1% (v/v) formic acid and 10 mM ammonium acetate in 50/50% ACN/H2O (B). Mass spectrometry was performed in positive ion electrospray (ESI+) modes.

**Results:** HILIC-MS metabonomic analysis was implemented on urine (n = 215) and faeces (n = 187) from healthy, CD and UC participants. Metabolite features were extracted from UPLC-MS data (urine n = 779, faeces n = 1888) and aligned across samples. Before multivariate statistical analysis, intensity coefficient of variations (CVs) of each metabolite feature were calculated and applied as filter (CV < 30%, urine n = 533 faeces n = 1065). Partial least square-discriminant analysis (PLS-DA) scores plot was performed to reduce the dimensionality of the data and to assess the relation between the participant groups. Classes for the supervised discrimination of the data were set according to each of the three groups. Various models were created; 1) healthy vs. DC, 2) healthy vs. UC and 3) CD vs. UC. For urine samples, the three models explained >90% of the variance ($R^2$) with strong predictive capacity ($Q^2$) >60–80% of the variance. For fecal samples, the three models explained >90% of the variance ($R^2$) and good predictive capacity ($Q^2$) >30–70% of the variance. On further PLS-DA, we were able to show that polar metabolities account for differences between UC and CD. PLS-DA analysis scores plot aimed also to decipher the progression of metabolic metabolism during anti-TNF treatment at 3 monthly interval (5 visits) (See Table 1). The biological effects of anti-TNF therapy on HILIC compounds can be seen by the strength of association as demonsrated by the most significant model between visit 1 and visit 3 in urine (R2 = 1, Q2 = 0.598) and falls away by visit 5 (R2 = 0.976, Q2 = 0.205). This may demonstrate that it may take approximately 6 months (at visit 3) before maximal host metabolism alterations occurs, at which time determination of response or non-response can be made. This is in contrast to faecal metabolites where there was a longer time to derivation of anti-TNF effect with maximal association at visit 5 (R2 = 0.957, Q2 = 0.494).

**Table 1:** The strength of assocation between CD patient visits.

| R2/Q2 | | V1 | V2 | V3 | V4 | V5 |
|---|---|---|---|---|---|---|
| Urine | V1 | - | 0.917/0.184 | 1/0.598 | 0.997/0.381 | 0.976/0.205 |
| | V2 | 0.917/0.184 | - | 0.968/0.119 | 0.983/0.128 | 0.955/0.116 |
| | V3 | 1/0.598 | 0.968/0.119 | - | 0.997/0.217 | 0.993/0.505 |
| | V4 | 0.997/0.381 | 0.329/0.128 | 0.997/0.217 | - | 0.997/0.252 |
| | V5 | 0.976/0.205 | 0.955/0.116 | 0.993/0.505 | 0.997/0.252 | - |
| Faeces | V1 | - | - | 0.996/0.360 | 0.906/0.421 | 0.957/0.494 |
| | V3 | 0.996/0.360 | - | - | 0.997/0.686 | 0.980/0.640 |
| | V4 | 0.906/0.421 | - | | - | 0.999/0.563 |
| | V5 | 0.957/0.494 | - | 0.980/0.640 | 0.999/0.563 | |

**Conclusion:** IBD phenotypes (UC and CD) have different polar metabolite profiles. Our data demonstrate that the biological effects of anti-TNF therapy in faecal and urine samples on host metabolism may be as late as 6 to 9 months. Identification of specific metabolites resulting in these differences will hope to develop biomarkers for future validation.

**Disclosure of Interest:** N.S. Ding: Abbvie - advisory board Falk - advisory board. P. Hendy: Abbvie - advisory board Falk - advisory board.
All other authors have declared no conflicts of interest.

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### P0271 FINGER CLUBBING: HIGH PREVALENCE IN SEVERE SMALL BOWEL CROHN'S DISEASE IN A PROSPECTIVE SINGLE-CENTER STUDY


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**Introduction:** Finger clubbing has been associated with Crohn's Disease (CD) since 1960s (1, 2). However, whether finger clubbing may represent a marker of aggressive CD course is undefined.

**Aims & Methods:** In a prospective single-center study, we aimed to assess whether finger clubbing in CD is associated with clinical characteristics of the disease. In particular, we aimed to investigate whether finger clubbing may represent a non-invasive marker of severe CD: From January to April 2016, CD patients (pts.) undergoing clinical assessment were enrolled. Inclusion criteria: 1) Diagnosis of CD; 2) Regular follow up (≥2 visits/yr); 3) Scheduled visit; 4) Age >18 yrs; 5) Clinical records including detailed clinical history. For each pt., the following characteristics were recorded: 1) Date of birth and of diagnosis of CD; 2) CD site (L1-L4) (3); 3) CD pattern (B1-B3) (3); 4) CD-related surgery; 5) CD duration; 6) Current/past use of thiopurines (IS) and/or anti-TNFα; 7) Smoking habits; 8) Pulmonary diseases. Finger clubbing was assessed by ≥2 IBD-dedicated gastroenterologists, and documented by photographic verification. Results were expressed as median (range).

**Results:** During the 4 months follow-up, 114 CD pts. The median age at time of the visit was 46 (18–79), at time of diagnosis of CD was 26 (12–72) and CD duration was 12 years (1–56.). CD lesions involved the ileum in 107 pts. (93.8%) (including: the ileum only n = 61; ileum-colon n = 31; jejunum.ileum n = 6; duodenum, stomach or esophagus and ileum: n = 9), or the colon only in 7 pts. (6.2%), Perianal CD was recorded in 23 (20.1%) and previous surgery in 60 (52.6%) pts. (>1 resection: n = 23 [38.3%]). IS use was observed in 57 pts. (50%), anti-TNFα in 42 (36.4%), both IS and anti-TNFα in 27 (23.6%) pts. Pulmonary diseases were observed in 10 (8.7%) pts. Finger clubbing was detected in 20 (17.5%) pts. Among the 20 pts. with clubbing, CD involved the ileum in 19 (95%) (also including the colon in 4 [20%]; jejunum in 4 [20%], the esophagus, stomach or duodenum in 1 [5%] pt.) and the colon only in 1 (5%) pt. Among the 20 CD pts. with finger clubbing, known history of:perianal CD was observed in 6 (out of 19: 31%). CD-related surgery (≥1) was observed in 14 (70%) and ≥1 resection in 4 (20%) pts. Defined IS use was observed in 12 (63.1%) CD pts. with finger clubbing, anti- TNFα in 9 (47.3%) and both treatments in 9 (47.3%) pts. Pulmonary diseases were recorded in 1 (5%) CD pts. with finger clubbing.

**Conclusion:** In the tested population, a high prevalence of finger clubbing was observed, particularly in CD pts. with extensive small bowel lesions requiring immunomodulators, The detection of finger clubbing may represent a non invasive marker of severity of CD.

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L. Biancone: No conflict of interests related to the study. This study was not sponsored. LB received lecture fees from Zambon, MSD, Takeda, Abbvie, Sofar. All other authors have declared no conflicts of interest.

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### P0272 PREVALENCE OF ULTRASONOGRAPHIC LOWER AND UPPER ENTHESITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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**Introduction:** Spondyloarthritis (SpA) occurs in up to 20% of patients with inflammatory bowel disease (IBD) [1]. Symptomatic enthesitis is a characteristic feature of SpA and represents an early sign of SpA [2]. The prevalence of enthesitis in patients with IBD is not known.

**Aims & Methods:** This study was designed to evaluate whether patients with IBD showed an increased prevalence of entheseal involvement, even in the absence of clinical symptoms. Thirty-five IBD patients (25 M and 10 F, median age 41 yrs), 25 with Crohn's disease (CD) and 10 with ulcerative colitis (UC), all with moderate intestinal activity, and 22 (13 M and 12 F, median age 44 yrs) control subjects with irritable bowel syndrome underwent a thorough clinical evaluation followed by entheses ultrasonography of upper limb (brachial triceps) and lower limb (quadriceps, proximal and distal rotuleus, Achilles tendon and plantar fascia). The Madrid sonographic entheses index (MASEI) was used to score entheses abnormalities [thickness, enthesophytosis, bursitis, erosions with and without power doppler (PD)]. Correlation between IBD features (type, duration and activity), age, sex and MASEI score was assessed with nonlinear Spearman's rho. Significance of differences was assessed by chi-square test. The level of statistical significance of differences was set at $p < 0.05$.

**Results:** All of 35 patients with IBD presented at least one entheses alteration with a mean MASEI of 5.43 (thickness 57.1%, enthesophytosis 42.8%, bursitis 0%, erosions 0%, PD abnormalities 14.2%) vs 3 patients of control group (enthesophytosis 14%) ($p < 0.05$). MASEI significantly correlated with the age of IBD patients ($p < 0.0001$).

**Conclusion:** 1) IBD patients showed a significantly higher prevalence of early entheses involvement, even in the absence of clinical symptoms; 2) the entity of entheses alteration as assessed by MASEI did not correlate with type, duration and activity of IBD; 3) age was the only variable which significantly correlated with ultrasonographic entheses involvement.; 4) we speculate that IBD patients should undergo ultrasonography evaluation of entheses and, if any alteration, be followed up for early detection of SpA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0273 COMBINED PET/MR ENTEROGRAPHY FOR THE NON-INVASIVE ASSESSMENT OF INFLAMMATORY ACTIVITY IN CROHN'S DISEASE

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**Introduction:** To assess the performance of combined PET/MR enterography in the assessment of inflammatory activity in Crohn's disease (CD).
**Aims & Methods:** N = 38 patients with Crohn's disease underwent PET/MR enterography with [18F]Fluorodeoxyglucose (FDG) using an integrated PET/MR scanner. For bowel distension an oral contrast solution (1500 cc of mannitol and locust bean gum) was ingested. The MR protocol comprised: 1) TrueFISP cor; 2) T2w HASTE fs cor and ax.; 3) dyn. T1w VIBE cor post gadolinium; 4) T1w FLASH 2D cor and ax post gadolinium as well as 5) EPI DWI ax (b = 0, 500, 1000). PET was acquired for 8 min per bed position. The datasets were reviewed by two readers in consensus regarding the presence of active inflammation. For each segment of the lower gastrointestinal tract SUVmax as well as SULmax (SUVmax/SUVmaxLiver) was determined. Ileocolonoscopy with a segment-based analysis served as standard of reference. ROC analysis for SUVmax and SULmax was performed to determine an optimal cutoff value. Furthermore, accuracy, sensitivity and specificity for PET, MRI and combined PET/MR were determined.
**Results:** In n = 38 pts (male n = 15; mean age: 42.4 ± 14.0; mean time since first diagnosis: 12 years; smoker n = 8), 219 ileocolonic segments were evaluated. According to the reference standard, active inflammation was present in 33 segments. A cutoff value for SULmax of >1 was associated with the highest accuracy (SULmax > 1: 0.78; SULmax > 1.5: 0.66; SULmax > 2: 0.74; SULmax > 3: 0.64) for the detection of inflammation. Using a cutoff value of SULmax < 1 sensitivity for PET was 88%, specificity 76%. MRI alone was associated with a higher specificity (sensitivity: 75%, specificity: 96%). Compared to MRI alone the combination of PET and MRI lead to an increase in sensitivity as well as decrease in specificity (sensitivity: 88%, specificity: 87%).
**Conclusion:** In combined PET/MR enterography FDG-PET as well as the MR data provide complementary information for the non-invasive assessment of inflammatory activity. In the present study the combination of PET with MRI lead to an increase in sensitivity. Combined PET/MR enterography allows for a multimodal and non-invasive assessment of inflammatory activity in Crohn's disease.
**Disclosure of Interest:** J. Langhorst: Research grant: TechLab, Steigerwald, Falk Foundation Lecture honorarium: Falk; MSD; Repha; Ardeypharm.
All other authors have declared no conflicts of interest.

## P0274 PRO-MC COLLABORATION: ESTABLISHMENT OF A PROSPECTIVE REGISTRY FOR MICROSCOPIC COLITIS IN EUROPE – A UEG LINK AWARD PROJECT

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**Introduction:** Microscopic colitis (MC) is an invalidating inflammatory disorder of the colon with chronic, watery, non-bloody diarrhea being the main symptom. To date, the disease course of microscopic colitis is largely unpredictable. Small, retrospective studies point towards an intermittent or chronic disease course, with only low rates of spontaneous remission. However, prospective studies on the disease course of MC are lacking and valid markers to predict the disease course at diagnosis have not yet been identified. To adequately assess the disease course of MC, a large and preferentially non-selected patient cohort is required. Considering the variable incidence rates of MC across Europe, international collaboration is indispensable.
**Aims & Methods:** The aim of the PRO-MC Collaboration is to systematically and prospectively collect data on the long-term disease course of MC and to improve the knowledge on MC across Europe. By a systematic brainstorm and selection process within an expert panel, the outcomes of interest were formulized, i.e. the persistence, respectively recurrence of diarrhoea and health-related quality of life of incident MC cases following diagnosis, the outcome of the treatments applied, and the characteristics of budesonide non-responders. Hereafter, a consensus on a follow-up strategy was reached and case record forms (CRFs) were drafted. Based on the CRFs, a web-based registry was built. Because pathology assessment is crucial for the diagnosis of MC, a slide kit presenting the diagnostic criteria and recommended stains was developed in collaboration with members of the European Society of Pathology (ESP), in order to increase the awareness of MC among pathologists and to improve data validity. All European MC centres can participate in the project and all new cases of MC in the participating centers are eligible for inclusion.
**Results:** For follow-up, a strategy with fixed visits was preferred. Patient data will be collected at diagnosis and at follow-up. Follow-up visits are scheduled 3, 6, and 12 months after diagnosis, yearly thereafter, and in case of clinical relapse. The CRFs include variables on demographics, symptoms, medical history, drug use, endoscopy and histology, disease activity, quality of life, comorbidity, treatment, and complications. All data will be recorded in a fully customized, web-based data registry. Disease activity and quality of life scores will be documented using a one week defecation diary and the Short Health Scale questionnaire.
**Conclusion:** The PRO-MC Collaboration, initiated with support of the UEG LINK Award, used a standardized approach to develop case record forms and a follow-up strategy, incorporated in an international, web-based registry for MC patients. The registry will generate novel insight into the long-term disease course of MC, and could possibly identify markers to predict the disease course and treatment outcome. The systematic, Europe-wide data collection will enhance the applicability of the project results and increase the awareness for the disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0275 A HISTOLOGICAL APPRAISAL OF HEPATOBILIARY DISORDERS IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** Diseases of the liver and biliary tract do occur in Inflammatory Bowel Disease (IBD) patients. In fact, in the clinical management of IBD patients, liver complications are of major concern as up to 30% of patients present with abnormal liver function tests. These abnormalities may be associated with IBD itself or be secondary to metabolic/physiological changes induced by IBD or drugs used during treatment.
**Aims & Methods:** We aimed to analyse and characterize the spectrum of hepatobiliary disorders in patients with IBD who underwent liver biopsy (LB) due to sustained altered liver function tests. Retrospective study of IBD patients who underwent LB between 2010 and 2015 due to sustained altered liver function tests at our tertiary referral centre. Demographic, clinical, laboratory, imaging and histological data were collected. Sustained altered liver function tests was defined as elevation for at least 6 months of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyl transferase (GGT), alkaline phosphatase (ALP) or total bilirubin.
**Results:** We included 54 patients (65% male, 34 with Crohn's disease) with a mean age of 43 ± 12 years. Mean time between the beginning of liver function tests abnormalities and LB was 12 ± 9 months. Eighteen percent of patients were under mesalazine, 39% under azathioprine and 43% under combination therapy (immunomodulators + anti-TNF-$\alpha$ agents). Twenty-eight patients had isolated elevation of transaminases, 11 patients cholestasis and 15 patients a mixed pattern. The aetiology of altered liver function tests was drug toxicity in 19 cases, non-alcoholic fatty liver disease (NAFLD) in 13 cases, and autoimmune hepatitis in 9 cases (66.7% induced by anti-TNF-$\alpha$ agents). We also identified 6 cases of primary sclerosing cholangitis (PSC), 2 cases of primary biliary cirrhosis (PBC) and 1 case of overlapping syndrome PSC/AIH, secondary amyloidosis, hemochromatosis, nodular regenerative hyperplasia and A1AT deficiency.
**Conclusion:** Abnormal liver function tests in IBD patients had a widely range of aetiologies and, in a significant number of cases, histology was essential for reaching a correct diagnosis. Drug toxicity, NAFLD and autoimmune hepatitis were the most common hepatobiliary disorders in this cohort of IBD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0276 EVALUATION OF QUALITY OF LIFE AND PAIN IN PATIENTS WITH ULCERATIVE COLITIS USING IBDQ, SF-36 AND EQ-5D – FIRST STEP OF PERSONALIZATION OF TREATMENT

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**Introduction:** In the last few years it was proven that the inflammatory bowel diseases (IBD) influence the quality of life (QL) of patients. Takin into account the clinical and endoscopic activity has proven insufficient. More often observation through patient report outcomes and evaluation of QL through different questionnaires are being used.
**Aims & Methods:** The aim was to evaluate the QL in patients with ulcerative colitis (UC) via - IBDQ, SF-36 and EQ-5D, and the influence of pain on this evaluation. **Material and method.** This covers 74 patients with UC, 41.9% men and 58.10% women, average age 43.9 12. All patients answered IBDQ, SF-36 and EQ-5D. We analyzed the overall evaluation of QL, the factors that influence the formation and the evaluation of pain/discomfort according the questionnaires used.
**Results:** The average QL evaluation according to IBDQ is 151.95 ± 44.15. The minimal evaluation that our patents give is 52 and the maximal 222. 37.8% of patients gave evaluation of 170 (typical of remission).

**PO276: Table 1:** Severity of the disease and QL (IBDQ).

| Severity | Total QL | Emotional state | Questions concerning the disease | Social aspects of life | General questions |
|---|---|---|---|---|---|
| **In remission** | 176.23 ± 38.39 | 61.23 ± 16.39 | 59.13 ± 12.25 | 29.42 ± 6.55 | 26.45 ± 6.02 |
| **Mild** | 159.28 ± 36.12 | 55.85 ± 15.23 | 52.14 ± 13.26 | 26.14 ± 7.42 | 25.14 ± 4.55 |
| **Moderate** | 137.85 ± 32.93 | 46.23 ± 14.54 | 46.54 ± 9.01 | 22.62 ± 8.11 | 22.46 ± 5.78 |
| **Severe** | 109.94 ± 34.93 | 40.87 ± 13.07 | 36.56 ± 12.56 | 16.50 ± 7.77 | 16.00 ± 5.74 |
| **Severity** | General health | Physical functioning | Physical role functioning | Intensity of pain | General health dimension |
| **In remission** | 54.55 ± 5.35 | 26.48 ± 4.03 | **7.69 ± 2.26** | **3.89 ± 1.85** | 16.48 ± 2.27 |
| **Mild** | 53.93 ± 4.65 | 25.50 ± 4.83 | **5.93 ± 1.73** | **5.07 ± 2.52** | 17.42 ± 2.21 |
| **Moderate** | 52.44 ± 4.18 | 25.00 ± 3.90 | **6.00 ± 1.65** | **4.44 ± 1.58** | 17.00 ± 2.23 |
| **Severe** | 53.06 ± 5.43 | 23.33 ± 4.83 | **4.80 ± 2.26** | **6.73 ± 2.57** | 18.20 ± 2.45 |
| **Severity** | General mental state | Vitality | Social functioning | Emotional role functioning | Mental health |
| **In remission** | 45.58 ± 3.50 | 17.89 ± 7.06 | 6.31 ± 1.03 | **5.58 ± 1.78** | 19.65 ± 2.62 |
| **Mild** | 45.14 ± 5.43 | 22.21 ± 9.05 | 5.93 ± 0.99 | **4.85 ± 1.40** | 19.57 ± 2.84 |
| **Moderate** | 44.11 ± 2.47 | 24.11 ± 9.64 | 5.77 ± 0.83 | **4.66 ± 1.41** | 19.33 ± 1.41 |
| **Severe** | 44.20 ± 4.17 | 17.89 ± 7.06 | 5.60 ± 0.82 | **3.80 ± 1.15** | 19.93 ± 2.08 |

The factor, that the most influences negatively all the used questionnaires for evaluation of QL - IBDQ, SF-36 and EQ-5D, is pain intensity ($p < 0.001$).

**Conclusion:** The intensity of pain, the duration and severity of UC are the main factors that influence the QL negatively. The use of questionnaires to evaluate the QL is useful in everyday practice, as they improve the complex idea on the development of UC and its effect and treatment on the patients and can help with the personalization of the UC treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0277 CROSS-SECTIONAL STUDY OF THE LOW SERUM CONCENTRATIONS OF TESTOSTERONE IN IBD AND THE INFLUENCE ON DISEASE ACTIVITY

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**Introduction:** Sex differences in the incidence and progression of inflammatory bowel diseases (IBD) have been reported in observational studies. The effect of testosterone on the pathogenesis of IBD is unknown.
**Aims & Methods:** The aim was to assess the serum concentration of testosterone in IBD male patients, to describe the prevalence of low serum concentration of testosterone and to investigate the effect of testosterone on disease activity. The cohort consisted of 113 consecutive IBD male patients (66 CD and 47 UC) examined at a tertiary IBD centre. Clinical and demographic characteristics of every patient were recorded, i.e. age, duration of the disease, clinical behaviour, location of disease according to Montreal classification, IBD related surgeries, concomitant medications. We measured the morning serum concentration of testosterone, luteinising hormone, cortisol, ACTH, CRP, vitamin D in each patient. Disease activity was assessed by Harvey-Bradshaw Index (HBI) in CD patients and by partial Mayo score in UC patients. The prevalence of low serum concentration of testosterone below the cut-offs 6 nmol/l and 10 nmol/l was assessed and risk factors analysed by univariate analysis.
**Results:** The median serum concentration of testosterone both in CD and UC male patients was 11 nmol/l. The low serum concentration of testosterone with cut-offs $\leq$6.0 nmol/l and $\leq$10.0 nmol/l was noted in 4/113 (3.5%) IBD male patients (3 CD and 1UC) and in 38/113 (33.6%) (22CD and 16UC), respectively. We found significant negative correlation between age and testosterone in all patients ($r2 = 0.067$, $p = 0.006$) and between CRP and testosterone in CD males ($r2 = 0.073$, $p = 0.028$). No similar correlation was seen in UC patients. We did not observe any significant correlation between clinical activity although there was a trend towards significance in correlation of partial Mayo score and level serum concentration of testosterone in UC males ($r2 = 0.076$, $p = 0.061$). Patients who undergone appendectomy had significantly lower serum concentrations of testosterone in comparison to those who did not with median of 11.3 vs 8.4 nmol/l ($p = 0.005$).
**Conclusion:** The prevalence of low serum concentration of testosterone was observed in 3.5% (cut-off $\leq$ 6.0 nmol/l) and 33.6% (cut-off $\leq$ 10.0 nmol/l) of IBD male patients. Serum concentration of testosterone correlated with age in all IBD patients and CRP in CD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0278 TOWARDS A PROACTIVE THERAPEUTIC DRUG MONITORING OF INFLIXIMAB - ASSESSMENT AND VALIDATION OF A NEW POINT-OF-CARE QUANTIFICATION DEVICE

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**Introduction:** Therapeutic drug monitoring (TDM) is a powerful strategy known to improve the clinical outcomes and to optimize the health care resources in the treatment of Inflammatory Bowel Diseases (IBD). Infliximab, a Tumour Necrosis factor (TNF) antagonist, is known to have an optimal therapeutic window of 3 to 7 $\mu$g/ml. However, most of the methods that are commercially available for the quantification of IFX are ELISA-based, and the results take approximately 8 hours to be obtained, delaying the target dosage-adjustment to the following infusion.
**Aims & Methods:** Our aim was to assess the performance and to validate the first point-of-care (POC) IFX quantification device available in the market by comparing it with two well-established ELISA methods. The POC IFX quantification device and the two established ELISA methods were used to assay the IFX concentration in the serum of 299 patients under IFX maintenance therapy. The results were statistically compared both in quantitative and qualitative terms.
**Results:** The Intraclass Correlation Coefficients (ICC) of the POC IFX assay compared with each of the two ELISA-based established methods were 0.889 and 0.939. The results were stratified according to the IFX therapeutic window ($<$3, 3–7 and $>$7), and the accuracy of the POC IFX compared with each of the two reference methods was 77% and 83%, whereas the kappa (95% CI) statistics were 0.648 (0.577–0.719) and 0.738 (0.673–0.803).
**Conclusion:** Our conclusions support that the newly launched POC IFX assay can successfully and effortlessly replace the commonly used ELISA-based IFX quantification kits. The fact that this POC IFX assay is able to deliver the results within 15 minutes makes it ideal for an immediate target concentration adjusted dosing. Moreover, it does not require specific laboratory facilities nor highly specialized personnel, being a user-friendly desktop device that holds the potential to revolutionize the TDM in IBD patients undergoing IFX therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0279 ADHERENCE TO RECOMMENDATIONS AND QUALITY OF ENDOSCOPIC COLORECTAL CANCER SURVEILLANCE IN LONG-STANDING ULCERATIVE COLITIS

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**Introduction:** Long-standing ulcerative colitis has been associated with an increased risk of colorectal cancer (CRC). Current guidelines recommend endoscopic CRC surveillance after 8 years of disease duration and then every 1–2 years (1). Use of chromoendoscopy has been recommended in order to increase precancerous lesions detection rates (1). There are currently few studies that assess adherence of clinicians to surveillance guidelines in the context of inflammatory bowel disease. The objectives of our study were to assess the adherence to recommendations and the quality of endoscopic procedure in long-standing ulcerative colitis.
**Aims & Methods:** This is a retrospective cohort study. We selected patients included in the Swiss IBD cohort having the following characteristics: left-sided colitis or pancolitis, disease duration >= 8 years, having experienced at least one period of remission during the follow-up. Patients with PSC were excluded. Complementary medical charts review focused on endoscopy and associated histological reports. Descriptive analyses were performed by first focusing on the patients and on the history of their colonoscopies. We then focused on the colonoscopies themselves.
**Results:** 391 colonoscopies were conducted among a total of 94 patients. Characteristics of patients at 8 years of disease duration were: men (51.1%), age at diagnosis (mean = 30.5, SD = 11.9), disease location at diagnosis (pancolitis 46.8%, left-sided colitis 38.3%, proctitis 6.4%, unknown 8.5%). Explicit indication for cancer screening was mentioned in 35.6% of colonoscopies. 40.6% of patients had a first screening colonoscopy before 8 years (resp. 53.6% before 10 years). Mean (SD) time since the next screening colonoscopy was 2.4 (1.5) years. Caecal (resp. ileal) intubation was performed in 85.2% (resp. 74.9%) of cases. Bowel preparation was good to excellent in 48.6% of endoscopies. Mean withdrawal time was 15.8 (10.6) minutes. Chromoendoscopy (virtual chromoendoscopy) was used in 2.6% (10%) of cases. Mean number of colonic biopsies was 14 (SD = 9.8, interquartile range = 18-7). Dysplasia/DALM was found in 14 cases (3.6%). Histologically confirmed adenomas were found in 13 cases (3.3%).
**Conclusion:** Despite current international recommendations, a significant number of patients were not included in a surveillance program. Patients undergoing surveillance colonoscopy were often inadequately prepared and chromoendoscopy was used in a minimal number of patients. Moreover, the number of biopsies was too low given that chromoendoscopy was not used. Overall, our data suggest that adherence to surveillance guidelines and endoscopic quality should be promoted and standardized.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0281 FECAL CALPROTECTIN LEVEL LOOKS PROMISING IN IDENTIFYING ACTIVE DISEASE IN BEHÇET'S SYNDROME PATIENTS WITH GASTROINTESTINAL INVOLVEMENT: A CONTROLLED AND PILOT STUDY

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**Introduction:** The fecal calprotectin (FC) is widely used as a non-invasive method for identifying patients with active Crohn's disease (CD) and ulcerative colitis. Gastrointestinal involvement of Behçet's syndrome (GIBS) shows clinical and endoscopic similarities to CD. A previous study in a small number of Behçet's syndrome (BS) patients with mainly mucocutaneous lesions showed serum calprotectin levels did not differ between active and inactive patients (1). Another study suggested FC may help to diagnose GIBS patients (2). We are not aware of studies addressing whether FC helps to distinguish active GIBS patients from those in remission.
**Aims & Methods:** The aim of this study is to determine whether FC helps predict active disease in GIBS patients. We collected fecal specimens from 23 GIBS (11 M, 12 F and mean age 44 ± 9 yrs) patients before colonoscopy. The reasons for colonoscopy were assessing active disease in patients presenting with abdominal pain (with or without diarrhea) (n = 9) or confirmation of a remission in asymptomatic patients (n = 16). Four symptomatic and 3 asymptomatic patients had active ulcers by endoscopy. On the other hand, 5 symptomatic and 13 asymptomatic patients did not have ulcers. We also included 22 active and 25 inactive CD patients as controls. We used 150 µg/g as the cut-off for a positive FC level. We also looked at the correlation between FC and serum CRP levels, Crohn's disease activity index (CDAI) and disease activity index for intestinal Behçet's disease (DAIBD) scores.
**Results:** FC was > 150 µg/g in all of the 7 GIBS patients with ulcers compared to 4/16 of GIBS patients without ulcers (OR, 95%CI: 42 to 888). The mean FC was 1125 ± 800 µg/g (95%CI: 341 to 1908) among symptomatic patients with ulcers (n = 4) and 209 ± 213 µg/g (95%CI: 22 to 396) among symptomatic patients without ulcers (n = 5). On the other hand, the mean FC was 243 ± 73 µg/g (95%CI: 158 to 328) among asymptomatic patients with ulcers (n = 3) and 95 ± 160 µg/g (95%CI: 0.4 to 189) among asymptomatic patients without ulcers (n = 11). Among CD patients, 16/25 active patients and 3/22 patients in remission had FC level > 150 µg/g (OR, 95%CI: 11 to 49). There was a low correlation between FC and serum CRP levels (r = 0.3, p = 0.1), a moderate correlation between FC and CDAI scores (r = 0.5, p = 0.02) and very low correlation between FC and DAIBD scores (r = 0.01, p = 0.9). Among the 4 GIBS patients who had high FC levels despite being in remission for gastrointestinal (GI) involvement, 1 had active mucocutaneous lesions, 1 had concomitant macrophage activation syndrome, and 1 had polycythemia vera with trisomy 8. None of the patients were receiving NSAIDs that could increase FC levels.
**Conclusion:** Pending the study of more number of patients, FC may turn out to be a useful non-invasive tool for ruling out active GI lesions in asymptomatic GIBS patients. A high FC level demands caution for the presence of active ulcers especially in symptomatic patients, but whether the presence of other BS manifestations can cause false positive results remains to be studied.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0282 LIVER FIBROSIS EVALUATION BY TRANSIENT ELASTOGRAPHY (FIBROSCAN®) IN PATIENTS WITH INFLAMMATORY BOWEL DISEA

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**Introduction:** Hepatobiliary disease is one of the most common extraintestinal manifestations of inflammatory bowel disease (IBD). However, the true prevalence of clinically significant chronic liver disease in patients with IBD is not known and could be underestimated due to reliance on abnormal liver tests and/or liver biopsies. Transient elastography, FibroScan®, is a non-invasive, safe and effective technique to evaluate liver fibrosis.
**Aims & Methods:** Our aim was to evaluate the prevalence of clinically significant liver disease in IBD patients using transient elastography. Prospective study including IBD patients between January and April 2016. Demographic, clinical and therapeutic data were obtained. Liver stiffness was assessed by transient elastography (FibroScan®), performed by a single physician. The cut-off values for advanced liver fibrosis were (according to the METAVIR scoring system): F ≥ 2: 7.1 and F ≥ 3: 9.5 kPa.
**Results:** A total of 34 patients were included, 18 women (53%), mean BMI of 18.43 ± 2.5 kg/m$^2$. The mean age was 38.5.5 ± 12.5 years. 24 patients had Crohn's disease (70.6%), 8 ulcerative colitis (23.5%) and 2 patients had indeterminate colitis (5.9%). Mean duration of disease was 4.5 years. The median value of liver stiffness was 4.5 kPa, the median IQR was 0.7 ± 0.2, with a mean success rate of 96 ± 5%. According to the cut-off value of 7.1 kPa, there were 33 patients (97%) with F < 2, and 1 patient (3%) with F ≥ 2. No patient had F ≥ 3.
**Conclusion:** Development of liver fibrosis in IBD patients is exceptional. FibroScan is a non-invasive and safe technique, which may be potentially useful for evaluation and follow-up of liver fibrosis in IBD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0283 CORRELATION OF FECAL CALPROTECTIN AND LACTOFERRIN LEVELS WITH ULCERATIVE COLITIS ENDOSCOPIC INDEX OF SEVERITY AND MAGNIFYING ENDOSCOPIC STRATIFICATION IN PATIENTS WITH ULCERATIVE COLITIS IN CLINICAL REMISSION

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**Introduction:** Recently, fecal markers such as calprotectin, lactoferrin, and hemoglobin have been reported to correlate well with the Mayo endoscopic subscore (MES) and expected to be used as an alternative monitoring tool to endoscopy. Ulcerative colitis endoscopic index of severity (UCEIS) is a newly proposed and more detailed endoscopic scoring system compared with MES; however, only few studies have examined the association between fecal markers and UCEIS. Recently, we proposed magnifying endoscopic stratification (ME) based on alternations in the mucosal surface pit patterns and showed its utility in predicting relapse in patients with ulcerative colitis (UC).
**Aims & Methods:** In this study, we investigated the association between the aforementioned fecal markers and MES, UCEIS, and ME in patients with UC in clinical remission. We included 39 patients with UC in clinical remission who underwent colonoscopy at the Nagasaki University Hospital between June 2015 and March 2016; their stool samples were collected on the same day as that of colonoscopy. Calprotectin and lactoferrin levels were measured using enzyme-linked immunosorbent assay. Clinical remission was defined as a partial UC-disease activity index score of ≤2 and a bloody stool score of 0. Furthermore, endoscopic remission and relapse was defined as an MES of ≤1 and ≥2, respectively.

**Results:** There were 12, 18, 9, and 0 cases with an MES score of 0, 1, 2, and 3, respectively. The endoscopic relapse rate was 23.1% (9/39 patients). A significant correlation was observed between MES and all fecal markers (Spearman's rank correlation coefficient: calprotectin 0.45, P = 0.004 lactoferrin 0.46, P = 0.003; and hemoglobin 0.41, P = 0.009) as well as between UCEIS and all fecal markers (calprotectin 0.57, P = 0.0002; lactoferrin 0.52, P = 0.0006; and hemoglobin 0.41, P = 0.01). In addition, ME correlated significantly with calprotectin and lactoferrin levels but not with hemoglobin levels (calprotectin 0.56, P = 0.0006; lactoferrin 0.49, P = 0.0017; and hemoglobin 0.31, P = 0.077). Moreover, a significant correlation was observed between ME and UCEIS (Spearman's rank correlation coefficient: 0.80, P < 0.0001).
**Conclusion:** Fecal markers correlate with not only MES but also UCEIS and ME and can be predictive of subclinical relapse in patients with UC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0284 THERAPEUTIC DRUG MONITORING OF INFLIXIMAB AND ADALIMUMAB FOR DETECTION OF PATIENTS AT RISK OF LOSS OF RESPONSE IN INFLAMMATORY BOWEL DISEASE


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**Introduction:** Due to the high cost of therapeutic drug monitoring (TDM) of infliximab (IFX) and adalimumab (ADA) in inflammatory bowel disease, many algorithms have been proposed to optimize the use of the analysis. Most of them are based on the determination of drug levels and antibodies if patients show loss of response (LOR).
Besides patients who develop drug antibodies, some patients have drug serum levels below the therapeutic range that may present a relapse without evidence of antibodies. For economic impact analysis, it is important to know the percentage of patients that are at risk of LOR due to low serum drug levels, with or without the presence of drug antibodies.
**Aims & Methods:** The aim of this study was to calculate the percentage of patients at risk of loss of response due to low concentrations of IFX or ADA, analyzing all treated patients of a population, not only those who had experienced LOR. Methods: A cross-sectional study of a cohort of patients with IBD was carried out. Patients were included consecutively through visits to the hospital to receive IFX or ADA. Serum drug concentrations and drug antibodies were measured by an ELISA technique. Patients with IFX levels < 3 mcg/mL and ADA < 5 mcg/mL were considered at risk of LOR. Usually, if IFX is present in a sample, antibodies detection could be altered. Therefore, negative antibodies results in these samples are often classified as inconclusive. Anyway, patients with low serum drug levels due to inter-individual pharmacokinetic variations or drug antibodies, are at increased risk of LOR.
**Results:** The study included 100 patients, 79 patients with Crohn's disease and 21 with ulcerative colitis, 68 treated with IFX and 32 with ADA. Mean age was 39 [17–69] years. Azathioprine immunosuppressive therapy was used by 40% of the patients.
In the IFX group, 40 patients (58.8%) were at risk of LOR and 4 (21.9%) in the ADA group. Drug antibodies were detected in 25.0% and 28.6% of the patients in IFX and ADA groups respectively.
The total number of patients with drug serum level below the cutoff without detectable antibodies was 30 in the IFX group and 5 in the ADA (75.0% and 71.4% of patients out of therapeutic range respectively). Only 2 patients with azathioprine developed antibodies.
The proportion of patients detected at risk of loss of response was high (44.1% in IFX group and 15.6% in ADA group).
**Conclusion:** The percentage of patients at risk of LOR is high, mainly those treated with Infliximab. Although not always resulting in clinical deterioration, there is a significant number of patients who could benefit from pharmacokinetic monitoring, helping to optimize dosage and prevent relapses.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0285 HOME-TESTING OF FAECAL CALPROTECTIN USING THE IBDOC™ SYSTEM: A COMPARATIVE PILOT STUDY


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**Introduction:** Faecal calprotectin (FCAL) is a useful test for monitoring of inflammatory bowel disease (IBD) activity. Providing a stool sample in person to the hospital laboratory is an anecdotally unpopular method with poor uptake. A new FCAL kit (IBDoc™, Bühlmann) enables self-testing using a proprietary collection tube, camera smartphone and app. The aim of this study was to assess patient's adherence to, and experience of, a testing regimen using IBDoc™, as well as benchmarking the assay to the standard laboratory test.
**Aims & Methods:** After focussed training, participants were asked to test using IBDoc™ once a month for four months and provide a standard stool sample which was posted to the hospital laboratory overnight and refrigerated on receipt, to be tested with standard ELISA (Bühlmann). The following questionnaires were applied before and after testing: GAD-7 (anxiety), PHQ-9 (depression), IBD-control-8, Multi-dimensional Health Locus of control (MHLC) and Cognitive Behavioural Responses to Symptoms (CBSRQ). Patients were also asked to record their experiences and preferences for testing on a proprietary questionnaire. REC reference 15/WA/0168.
**Results:** 54 consecutive patients (Crohn's: 23, UC: 31, F = 28, mean age 36.0 ± 9.2 yrs) were enrolled. Participants completed a median of 3 tests (0–4) during the study with 19/54 (35%) completing all four set time points and 17/54 (32%) returning no samples, despite active reminders. There was no difference in any of the questionnaire scores between compliant and non-compliant patients. There was moderate correlation of numerical FCAL results between the two methods (r = 0.77, 95%CI 0.68–0.84, p < 0.0001). Categorising results into disease activity categories (no inflammation, mild, moderate, severe) produced a similar result (weighted $\kappa = 0.57$, p < 0.0001). 63% of respondents stated a preference for IBDoc™, but stated that (in a routine clinical scenario) they would require timely contact from the hospital team in the event of an abnormal result (24–72 hours). A further 22% of patients preferred the IBDoc™ test, but stated that they would not require contact until their next scheduled appointment.
**Conclusion:** There was reasonable uptake and adherence to a demanding testing regimen (more frequent testing than might be required in routine clinical care) with 85% of respondents preferring the IBDoc™ test over other methods. The home testing kit results show only moderate correlation to laboratory results. While this is a promising and clearly popular technology, further studies are warranted to correlate results to clinical outcomes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0287 TRABECULAR BONE SCORE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES


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**Introduction:** Osteopenia and osteoporosis are known chronic complications of inflammatory bowel diseases (IBD). It is known that areal bone mineral density (aBMD) does not sufficiently reflect bone strength and quality. The trabecular bone score (TBS) provides an indirect measurement of bone microarchitecture, independent of aBMD.
**Aims & Methods:** The aim was to assess TBS and BMD of lumbar spine (LS) in IBD patients. Furthermore we analyzed the impact of clinical factors on TBS. The cohort consisted of consecutive IBD patients from tertiary IBD centre. Clinical characteristics i.e. age, gender, anthropometry, clinical behaviour, medication were recorded. The BMD was determined by dual-energy X-ray absorptiometry (DXA, Hologic Discovery) at the lumbar spine. TBS was determined by TBS Insight® software (Medimaps, France).
**Results:** The cohort consisted of 84 IBD patients (53 with Crohn's disease (CD) and 31 with ulcerative colitis (UC)). The mean age was 42.0 ± 14.2 years with the mean disease duration of 11.0 ± 7.0 years. There were 14% (12/84) postmenopausal women, 8 patients (9.5%) were on long term corticosteroids and 21 CD patients had prior major IBD surgery. The percentage of patients with substitution of vitamin D (800 IU) and calcium (0.5–1 g) was similar between CD and UC (24.5% vs. 29.0%), none of the patients was on anti-porothic treatment. The mean LS BMD of the cohort was 0.964 ± 0.113 g/cm$^2$ and TBS 1.36 ± 0.14. We observed significantly lower mean TBS LS in patients with fistulising CD compared to luminal CD, 1.36 ± 0.09 and 1.47 ± 0.05 (p = 0.0039) respectively. No similar finding was observed using BMD. We did not observe any significant impact of clinical characteristics nor medication in UC patients.
**Conclusion:** We observed that TBS LS might identify quality of bone mineral density better than BMD itself, mainly in CD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0288 AN AUDIT OF ENDOSCOPY IN ULCERATIVE COLITIS; SHOULD ENDOSCOPY FOR INFLAMMATORY BOWEL DISEASE (IBD) BE PERFORMED BY AN IBD SPECIALIST?

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**Introduction:** Endoscopy plays a vital role in the management of Ulcerative Colitis (UC), both in terms of; 1. Accurate assessment of severity (at diagnosis and response to treatment) 2. Colorectal Cancer Surveillance (CCS) Endoscopic assessment is often performed by general endoscopists, rather than those with a special interest in IBD. We assessed the quality of endoscopy performed for patients with UC. In acute UC we assessed whether severity had been accurately determined as suggested by ECCO guidelines.1 For CCS we assessed adherence to BSG guidelines.2.

**Aims & Methods:** Colonoscopy and flexible-sigmoidoscopy reports were analysed over a 6-month period (1.05.15 – 31.10.15) at a London District General Hospital. In acute UC quality of reports were assessed by classifying into either a) utilisation of a recognized scoring system b) a qualitative assessment using descriptive terms appropriate to justify grading c) a simple description as mild/moderate/severe with no other assessment d) no assessment of severity. For CCS, the quality of procedure was assesssed by classifying into a) appropriate use of dye spray b) dye spray not used but justification given c) if dye spray not used then documentation of 2–4 biopsies taken every 10 cm as per BSG guidance d) non-adherence to BSG guidelines.

**Results:** Acute UC (n = 60).

| | Physician (n = 36) | Surgeon (n = 12) | Nurse endoscopist (n = 12) | All endoscopists (n = 60) |
|---|---|---|---|---|
| a) scoring system | 11 (31%) | 0 (0%) | 0 (0%) | 11 (18%) |
| b) qualitative disease assessment | 20 (55%) | 2 (16%) | 3 (25%) | 25 (42%) |
| a) or b) | 31 (86%) | 2 (16%) | 3 (25%) | 36 (60%) |
| c) classification as mild/moderate/sever e | 4 (11%) | 5 (42%) | 9 (75%) | 18 (30%) |
| d) no severity assessment | 1 (3%) | 5 (42%) | 0 (0%) | 6 (10%) |

CCS (n = 34) Pancolonic mucosal dye spraying was used in only 11 (32%) colonoscopies. There was an appropriate justification as to why dye spray was not used in a further 8 (24%) colonoscopies, namely poor bowel prep. Of those that didn't undergo dye spray, 0% had biopsies every 10 cm. 15 (44%) colonoscopies were non-adherent to BSG guidelines. IBD endoscopists adhered to the BSG guidelines 9/11 (82%), compared to general endoscopists 13/23 (57%).

**Conclusion:** In acute UC, use of a validated scoring system is low. Use of either a validated scoring system or good description of severity is good in physicians but poor in surgical and nurse endoscopists. In CCS overall adherence to BSG guidance was low, with a low use of dye spray and large inter-operator variability suggesting dependance on operator rather than patient factors. IBD endoscopists showed greater adherence to guidelines. Our results suggest a case for patients with UC in both scenarios to have endoscopies performed by endoscopists with a special interest in IBD and appropriate endoscopic skills.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0289 THE USE OF THE WHO FACTURE RISK ASSESSMENT TOOL (FRAX) IN PREDICTING RISK OF FRACTURES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW

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**Introduction:** Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is associated with an increased prevalence of osteoporosis and osteopenia. The fracture risk assessment (FRAX®) tool is a risk-assessment survey developed by the World Health Organization (WHO) that calculates the 10-year probability of hip fracture and major osteoporosis-related fracture (including clinical spine; forearm; hip or proximal humerus fracture). The WHO FRAX® score utilizes age, sex, body mass index, clinical risk factors, and femoral neck bone mineral density (BMD) to estimate the 10-year probability (of hip fracture and major osteoporosis-related fracture – repetitive). It is composed of 11 variables: age, sex, weight, height, previous fracture as an adult, parental hip fracture, current cigarette smoking, current (or 3 months prior) use of glucocorticoids, diagnosis of rheumatoid arthritis, consumption of ≥3 units of alcohol daily, and secondary osteoporosis. It can be used with or without the addition of the bone mineral density derived T-score at the femoral neck, but conflicting results have been provided regarding the reliability of FRAX estimation without BDM measurements.

**Aims & Methods:** Our research aims to conduct a systematic review to assess the 10-year risk of fracture as determined by the FRAX® tool in patients with IBD in order to provide an up-to-date summary of the available evidence on the utility of this tool in the prediction of bone fracture risk among these patients. Electronic searches were performed with keywords relating to IBD and FRAX in the MEDLINE, EMBASE and SCOPUS databases. Summary estimates were calculated. A fixed or random-effects model was used depending on heterogeneity ($I^2$).

**Results:** The search yielded 146 references; 7 that included research carried out in adult patients, were used in the systematic review and quantitative summary. No significant publication bias was noted according to the Harbord test. The 10-year probability of hip and major osteoporotic fracture in adult IBD patients was 1.03% (95% CI, 0.37% – 2%; $I^2$ 0%) and 4.05% (95% CI, 2.61% – 5.79%; $I^2 = 49\%$), respectively. In those patients with Crohn's disease, hip and major osteoporotic fractures calculated with FRAX increased to 1.74% (95% CI, 0.42% – 3.93%; $I^2 = 37.5\%$) and 6.65% (95% IC, 2.97% – 11.66%; $I^2 = 8.7\%$), respectively. Risks of fracture in adults with ulcerative colitis were provided by a single study only.

**Conclusion:** The FRAX tool has been limited to use in patients with IBD, however the evidence currently available only shows a modest increase in the 10-year risks of bone fracture and does not support unequivocally the need for specific interventions. Further well-designed studies are needed to confirm the results obtained from this systematic review.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0290 DEVELOPMENT OF A NOVEL ENDOSCOPIC SCORING SYSTEM PREDICTING THE RELAPSE AFTER SURGERY IN INTESTINAL BEHCET'S DISEASE

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**Introduction:** Behcet's disease (BD) is a multi-systemic vasculitic disorder featuring multi-organ involvement including gastrointestinal tract. Surgical therapy for intestinal Behcet's disease is considered for patients unresponsive to medical treatments or those with bowel complications. According to our previous studies, cumulative surgery rates of intestinal Behcet's disease is 6.7% and 15.1% after 2 and 5 years of diagnosis each, and the recurrence rate of intestinal lesions was approximately 50% at two years postoperatively. The idea is that an appropriate algorithm and scoring system involving follow-up endoscopic findings which can predict recurrence of intestinal Behcet's disease after intestinal resection needs to be developed.

**Aims & Methods:** This study aimed to establish a scoring system based on follow up endoscopic findings which can predict intestinal Behcet's disease recurrence after surgery. A total of 91 intestinal Behcet's disease patients who underwent surgical intervention due to complication of intestinal Behcet's disease in Severance hospital between March 1986 and December 2015 were identified retrospectively. Their medical records were reviewed by two physicians (JH Cheon and JW Park). Among them, 54 patients who underwent follow-up endoscopy within 5 year after surgery, regardless of clinical relapse, were selected. After selection, demographic and preoperative clinical data including follow up colonoscopic findings (ulcer location, distribution, shape, number and depth) were retrieved. Clinical relapse were defined as DAIBD over 40, existence of newly added medications or admission due to symptomatic aggravation, re-operation related to intestinal Behcet's disease. Univariate and multivariate analyses were performed to find clinically relevant factors associated with clinical relapse of intestinal Behcet's disease after surgery. Classification And Regression Tree (CART) analysis was used to discover the appropriate model of endoscopic classification which can explain the post-surgical recurrence of intestinal Behcet's disease most properly; e, 0 – no lesions; e, 1 – <20 mm sized solitary ulcer; e, 2 – 20 mm sized solitary ulcer; e, 3 – multiple ulcers regardless of size.

**Results:** Median age at diagnosis was 36 years (range 12–69) with 28 male and 26 female patients. Clinical relapse occurred in 37 patients (61.52%) and 16 patients (29.63%) underwent re-operation. 37 patients (61.52%) had colonoscopic recurrence at follow-up colonoscopy, and among these cases, only 28 cases had clinically relapsed. All colonoscopically recurred cases had ulcers located in the anastomosis site and 34 cases (91.9%) occurred in the localized area. Multivariate Cox hazard regression analysis identified younger age years) at diagnosis (HR = 0.26; 95% CI, 0.098–0.689, p = 0.007), disease duration (HR = 0.992, 95% CI, 0.984–1.0, p = 0.043), previous immunosuppressant usage such as azathioprine, 6-MP, cyclosporine (HR = 0.306; 95% CI 0.134–0.697, p < 0.001), continued immunosuppressant usage after surgery (HR = 3.678, 95% CI, 1.495–9.051, p = 0.005), higher DAIBD at colonoscopy (HR = 1.032, 95% CI, 1.019–1.045, p < 0.001) and colonoscopic recurrence (HR = 2.992, 95% CI 1.133–7.904, p = 0.027) as independent risk factors for clinical relapse in IBD. Endoscopic findings were classified in four groups, according to size and number of recurred ulcer (s), and multivariate analysis adjusting age at diagnosis, disease duration, previous surgical resection, medication and disease activity score showed that the endoscopic score was an independent risk factor of clinical relapse (p = 0.043).

**Conclusion: Conclusion** According to the results of our study, this new endoscopic scoring system could predict the clinical relapse of patients undergoing surgical resection due to complications of intestinal Behcet's disease. Nevertheless, a larger-scale prospective study is needed to validate this scoring system.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0291 SIGNIFICANCE OF SEROLOGICAL MARKERS IN THE DISEASE COURSE OF ULCERATIVE COLITIS

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**Introduction:** Data are few and conflicting regarding the association of serological markers to the disease behavior, medical treatment and response to therapy in patients with ulcerative colitis (UC). We aimed to determine the prognostic potential of serological antibodies regarding long-term disease course of an adult prospective UC patient cohort. The association between serological markers and requirements for immunosuppressant or anti-TNF therapy was also evaluated.

**Aims & Methods:** One hundred and eighty-seven consecutive patients (male:46.0%, median age:40 years, extensive colitis:33.3%) were studied from a single referral IBD center. Sera were tested for a panel of different IgA/IgG type autoantibodies (anti-neutrophil cytoplasmic[ANCA], anti-lactoferrin[aLFS], anti-goblet cell and anti-pancreatic [anti-GP2 and anti-CUZD1] antibodies) by IIFT and for anti-microbial antibodies (ASCA IgG/IgA and anti-OMPPlus$^{TM}$ IgA) by ELISA. Clinical data were available on unfavorable disease outcome as well as disease activity and medical treatment during the prospective follow-up (median: 104 months).

**Results:** A total of 73.6%, 62.4% and 11.2% of UC patients were positive for IgA/IgG type of pANCA, aLFS and anti-goblet cell antibodies, respectively. Both type of anti-pancreatic antibody occurred in 9% of the patients, while ASCA and anti-OMP in 17.7% and 19.8%. Serological antibody status was stable over time. There was no significant association between antibody positivity and gender, age at onset or disease extent. Presence of certain antibodies was negatively associated to the occurrence of extraintestinal manifestations: aLFS IgA/IgG to current smoking status (OR:0.26, $p = 0.01$) and ocular disease (OR:0.16, $p < 0.01$), while pANCA IgA/IgG to the arthritis (OR:0.36, $p = 0.026$). During the follow-up period, UC-related hospitalization occurred in 34.2% and requirement for colectomy was 3.7%. Exposure to steroids, azathioprine or anti-TNFs was 77.0%, 37.4% and 13.4%, respectively. IgA type ASCA and anti-CUZD1 antibody but not other serological markers were associated to an increased likelihood of requirements for immunosuppressant in Kaplan-Meier analysis (pLogRank $< 0.01$ for both), however only ASCA IgA was identified as an independent predictor in multivariate Cox- regression model (HR:2.74, 95%CI:1.46–5.14, $p < 0.01$) comprising age at onset, gender, disease extent as covariates. At the same time, clinical factors, such as extensive colitis and male gender were exclusively associated with UC related hospitalization, HR:1.8 (95%CI:1.09–2.95, $p = 0.019$) and HR:6.7 (95%CI:1.6–27.9, $p < 0.01$), respectively.

**Conclusion:** Present prospective study displays limited role of serologic markers in the prediction of disease course in UC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0292 INTER-OBSERVER AGREEMENT IN BOWEL ULTRASONOGRAPHY FOR DIAGNOSTIC ASSESSMENT IN PATIENTS WITH CROHN'S DISEASE

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**Introduction:** Bowel Ultrasonography (US) constitutes an attractive imaging modality in Crohn's disease (CD) because it can be repeated frequently to assess and monitor lesions over time. Bowel US does not involve radiation and its low cost provides an alternative to other techniques, especially for children and young patients. Currently, however, a lack of standardization of the bowel US parameters commonly used in CD and the still reduced number of skilled ultrasonographers in this technique is limiting the use of this imaging modality around the world.

**Aims & Methods:** The aim of this study was to assess the interobserver agreement among different sonographers, experts in bowel US, from different centers, in the evaluation of predefined bowel US parameters commonly used in the detection and follow-up of patients with CD in order to develop an unequivocal imaging interpretation.

Fifteen patients with established CD underwent bowel US performed blindly by 6 sonographers from different IBD centers around the world, expert in bowel US (>1000 exams/year). Before the evaluation, the operators and clinical and radiological IBD experts dedicated a meeting to formally define the US parameters [site lesion, bowel wall thickness (3–7 mm vs >7 mm), bowel wall pattern (preserved vs disrupted), vascularization (absent/mild vs moderate/severe), lymph nodes, mesenteric adipose tissue alteration, stenosis, fistulas, phlegmon and abscess) that have been included in the study. Interobserver agreements were tested with Fleiss' kappa statistics.

**Results:** Fleiss' k values were moderate for bowel wall thickness ($k = 0.54$, $p = 0.01$), site lesion ($k = 0.46$, $p = 0.01$), bowel wall pattern ($k = 0.43$, $p = 0.001$), vascularization ($k = 0.59$, $p = 0.001$) and mesenteric adipose tissue alteration ($k = 0.43$, $p = 0.001$). Agreement was good and excellent for prestenotic dilation and penetrating complications ($k = 0.73$–$1$, $p = 0.001$). Fair and poor agreements were observed for stenosis, lymph nodes and lesion extent ($k < 0.3$, $p = 0.001$).

**Conclusion:** In this pilot study most of the US parameters used in CD patients showed a satisfactory reproducibility. The development of a common US imaging interpretation among bowel sonographers will allow the better comparability of US results among various centers, improve the quality of multicenter US studies and bowel US training with a further diffusion of this technique.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0293 THE BRISTOL STOOL FORM SCALE AND A VISUAL ANALOGUE SCORE FOR ABDOMINAL PAIN MAY BE USED AS PATIENT REPORTED OUTCOME MEASURES IN CROHN'S DISEASE

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**Introduction:** Patient-reported outcomes are increasingly important disease measures in Crohn's disease.

**Aims & Methods:** We aimed to investigate whether (i) the Bristol Stool Form Scale (BSFS) and (ii) a visual analogue scale (VAS) for abdominal pain can be used as patient reported outcome measures in Crohn's disease. In this prospective cohort study, patients with active Crohn's disease were included before they started treatment with corticosteroids or TNF inhibitors. Patients with colectomy or stoma were excluded. The following parameters were collected prior to treatment and 10 weeks later: Harvey Bradshaw Index (HBI), Crohn's Disease Activity Index (CDAI), serum CRP and fecal calprotectin. At the same time points, participants completed a 7-day diary containing the following items for each day: BSFS (1–7) and 10 cm VAS for abdominal pain. HBI-response was defined as a reduction in HBI $\geq 3$; CDAI-response was defined as a reduction in CDAI $\geq 100$; calprotectin-response and CRP-response were defined as reduction of $\geq 50\%$ compared to baseline values. Changes in minimum, mean and maximum BSFS and changes in VAS score were evaluated in relationship to clinical and biochemical response using area under the receiver operator characteristic curve (AUROC). Guyatt's responsiveness statistic was calculated as the mean change in responders divided by the standard deviation of the change in non-responders. Test-retest reliability was evaluated using single measure intraclass correlation coefficients (ICCs).

**Results:** A total of 42 patients were included of whom 35 completed the study (31% males, mean age 41 years). Corticosteroids (6 prednisolone, 16 budesonide) were started in 63% and TNF inhibitors (6 infliximab, 7 adalimumab) in 37%. Clinical response based on HBI or CDAI was observed in respectively 38% and 24% of the patients, while CRP- and calprotectin-response was seen in 38% and 55% of patients, respectively. Change in the lowest BSFS-score and change in mean VAS-score were most strongly associated with HBI-response (respectively, AUROC 0.91, 95% CI 0.81–1.0; AUROC 0.92, 95% CI 0.82–1.0; Guyatt's statistic 1.06; 2.24) and CDAI-response (respectively, AUROC 0.90, 95% CI 0.79–1.0; AUROC 0.94, 95% CI 0.85–1.0; Guyatt's statistic 2.96; 2.24). Change in mean highest BSFS-score (AUROC 0.60, 95% CI 0.39–0.81) and change in highest VAS-score (AUROC 0.81, 95% CI 0.65–0.96) were most strongly associated with calprotectin-response; Guyatt's statistic 0.95 and 2.24, respectively. Change in mean lowest BSFS-score (AUROC 0.64, 95% CI 0.45–

0.84) and change in highest VAS-score (AUROC 0.70, 95% CI 0.50–0.90) most strongly associated with CRP-response; Guyatt's statistic 2.43 and 2.68, respectively. Test-retest reliability was moderate for VAS-score (ICC 0.70 and 0.58, before and after treatment, respectively), and moderate to strong for lowest (ICC 0.80 and 0.65), mean (ICC 0.75 and 0.52) and highest (ICC 0.51 and 0.50) BSFS-score.
**Conclusion:** The Bristol Stool Form Scale and a visual analogue scale for abdominal pain appear to be reliable, accurate and responsive instruments to evaluate the effect of treatment in patients with Crohn's disease. Future studies are required to validate whether these instruments can be used as outcome measures in Crohn's disease trials.
**Disclosure of Interest:** M. Löwenberg: Served as speaker and/or principal investigator for Abbvie, Covidien, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillotts and Tramedico. Received research grants from AbbVie, Merck Sharp & Dohme, Achmea and ZonMW.
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G.R.A.M. D'Haens: Please contact the author. 255 characters is insufficient: Abbvie, Ablynx, Actogenix, Amakem, Amgen, AM Pharma, AstraZeneca, Avaxia, Bristol Meiers Squibb, Boerhinger Ingelheim, Celgene, Celltrion, Cosmo, Covidien, Elan, Ferring, Dr Falk, Jansen, Engen.
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## P0294 PRESARCOPENIA SCREENING OF CROHN'S PATIENTS – GENDER AND BMI-SPECIFIC BODY COMPOSITION ASSESSMENT

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**Introduction:** Malnutrition and altered body composition (BC) can develop in patients with inflammatory bowel diseases for a variety of reasons.
**Aims & Methods:** Our aim was to develop a method to diagnose presarcopenia at an early stage in Crohn's disease (CD) outpatients, based on the assessment of body composition (BC) as well as using fat-free mass index (FFMI) reference values of the healthy population to prevent sarcopenia. The second aim was to establish national reference values for FFMI percentiles. 136 CD outpatients and 1752 healthy controls were included. Bioelectrical impedance analysing (BIA) method was used to measure BC. BMI and FFMI percentiles were determined within the healthy population, and cut-off point was established for the proposed presarcopenia screening method.
**Results:** BMI and FFMI were significantly different between the groups of patients and healthy subjects (median BMI: 22.0 vs 25.1 $kg/m^2$, $p < 0.0001$; FFMI: 17.3 vs 18.4 $kg/m^2$, $p = 0.0044$; respectively). Low BMI (i.e., malnutrition) was diagnosed among patients vs. healthy subjects for 32% vs. 4% for men and 33% vs. 13% for women; whereas low FFMI (i.e., presarcopenia) was diagnosed for 25% vs. 5% for men and 36% vs. 14% for women. Considering CD patients, both genders had almost the same prevalence of low BMI, but more females had low FFMI. Thus, a reasonable algorithm was suggested (based on BMI and FFMI) for nutritional intervention of CD outpatients to prevent severe malnutrition and sarcopenia.
**Conclusion:** BC assessment is essential for CD patients because of high risk for presarcopenia. Our study presents charts for BIA-determined gender-, age-, and BMI-specific percentiles for FFMI, based on healthy adults.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0295 CAPSULE ENDOSCOPY CROHN'S DISEASE ACTIVITY INDEX (CDEAIIC OR NIV SCORE) FOR THE SMALL BOWEL AND THE COLON

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**Introduction:** Crohn's disease (CD) is a chronic inflammatory disorder defined as a transmural inflammation of the bowel wall, affecting the small and large intestine. The Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv score) was devised to measure mucosal disease activity. We extended the Niv score to the colon and have a comprehensive view of the whole intestine of CD patients.
**Aims & Methods:** To establish a new capsule endoscopy score for disease activity in Crohn's disease of the small and large intestine. We evaluated 3 parameters of intestinal pathology: A. Inflammation B. Extent of disease C. Presence of strictures, for the proximal and distal small bowel, and for the right and left colon. The scoring formula is as follows: CEDCAIic = (A1 x B1 + C1) + (A2 x B2 + C2) + (A3 x B3 + C3) + (A4 x B4 + C4) (1 = proximal small bowel, 2 = distal small bowel, 3 = right colon, 4 = left colon).
**Results:** The median CECDAIic score was 15.5 (range 0 – 42), and the mean (±SD) score was 17.2 ± 11.5. The CECDAIic scores per patient were similar among the 5 observers. Kendall's coefficient of concordance was high and significant for almost all the parameters examined but for strictures in the proximal small bowel and distal colon. Nevertheless, the coefficients for the small bowel and for the whole intestine were high, 0.85 and 0.77, $P < 0.0001$, respectively.
**Conclusion:** We established a new score, the CECDAIic of the small-bowel and colonic CD. We offer this easy, user friendly score for use in randomized controlled trials as well as in the clinical follow-up of CD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0296 MUCOSAL HEALING: MAYO 0 VS 1 AFTER 3 YEARS

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**Introduction:** Mucosal endoscopic healing (MH), is considered the best prognostic factor in patients with ulcerative colitis (UC) but currently, there is no consensus regarding its definition1. Most of the studies define MH by a Mayo endoscopic score (MES) 0 or 1, others distinguish score 0 from score 1.
**Aims & Methods:** To measure the prognostic value of MES 0 and 1 in the prediction of the clinical course of patients with UC in stable clinical remission. Methods: Sixth-four patients with UC in stable clinical remission with high dosage of mesalazine were studied. All the patients underwent colonoscopy at baseline and MES was measured. Clinical course was evaluated measuring relapses needing steroids, immunosuppressants and/or biologics, after 3 years of follow-up. Statistical analysis was performed using the Kaplan-Meier life-table method, the log-rank test, the Cox's proportional hazard model, as appropriate.
**Results:** At the baseline, 36 patients (56%) showed a MES 0; 21 (33%) MES 1, 7 (11%) MES 2, none MES 3. At 3-year of follow-up, 50% of patients were still in remission. The cumulative proportion of steroid free remission at 36 months of follow-up in MES 0, 1 and 2 was 69%, 35%, and 0%, respectively ($p < 0.0001$ among all groups). Patients with MES 1 and 2, showed a hazard risk of relapse 2.86, and 15.74 times higher than those with MES 0 (table).

| MES | baseline | after 3 years | Hazard Risk |
|---|---|---|---|
| 0 | 36 | 25 | 1 |
| 1 | 21 | 7 | 2.86 |
| 2 | 7 | 0 | 15.74 |

**Conclusion:** Only the Mayo endoscopic score of 0 should be considered as mucosal healing.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### Reference

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## P0297 A POOLED SAFETY ANALYSIS FROM THE USTEKINUMAB CROHN'S DISEASE AND PSORIATIC DISEASES PHASE 2 AND 3 CLINICAL TRIAL PROGRAMS

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**Introduction:** Ustekinumab (UST) is a well-established therapy in psoriasis (PsO) and psoriatic arthritis (PsA) with up to 5 years safety experience from psoriasis clinical trials with 3117 pts & 8998 patient years (PY) of follow-up. However, limited safety data have been presented in Crohn's disease (CD). In pts with CD, Phase 2/3 data show that UST is safe & effective. Herein we present CD safety results & compare these with the safety profile in psoriatic diseases.
**Aims & Methods:** Safety data from 5 CD (2 Ph2/3Ph3) trials were analyzed with the previously reported PsO (1 Ph2/3Ph3) & PsA (1 Ph2/2 Ph3) randomized

controlled trials. All psoriatic pts received UST 45 or 90 mg SC; Ph3 CD pts received a single IV UST induction dose of 130 mg or ~6 mg/kg followed by 90 mg SC q8 or q12 wks. In PsO trials, no concurrent treatment was permitted; concomitant MTX was permitted in PsA trials & concomitant immunomosuppressives & corticosteroids were permitted in CD trials. All pts who received ≥1 dose of UST were included. Safety outcomes are presented as events per 100 PYs.
**Results:** Through the PBO-control period across all indications, 3636 pts were treated with UST (1582 PsO, 692 PsA & 1362 CD). Treated pts with ≥1 reported event PBO vs UST in pooled indications (incidence/100 PY of f/u): AEs 556.1 vs 594.3; SAEs 19.5 vs 16.4; infections 135.8 vs 138.1; serious infections 2.9 vs 3.3; MACE 0.26 vs 0.60; malignancies 0.26 vs 0.12; deaths 0 vs 0.12. Through 1 year, 5884 pts were treated with UST (3117 PsO, 1018 PsA, & 1749 CD) with 4521 PY of follow-up. Rates of AEs, SAEs, infection/serious infection were similar between UST group and PBO (Table) across the pooled indications. Event rates in the combined CD studies were also similar between treatment groups (PBO & UST groups) with overall AEs, & infections occurring more frequently in CD pts.
**Conclusion:** UST has a favorable safety profile in CD with IV induction dosing up to 6 mg/kg & SC maintenance dosing up to 90 mg q8wks. Evaluation of the CD experience did not alter the safety profile of UST previously defined in pts with psoriatic disease treated with up to 5 years of therapy.
**Disclosure of Interest:** S. Ghosh: Investigator for Janssen Research & Development, LLC.
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## P0298 SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF THE NOVEL ORAL PEPTIDE THERAPEUTIC PTG-100 (ALPHA4-BETA7 INTEGRIN ANTAGONIST) IN NORMAL HEALTHY VOLUNTEERS

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**Introduction:** PTG-100 is an orally administered, potent and highly selective $\alpha4\beta7$ antagonist peptide therapeutic that is being developed for the treatment of ulcerative colitis (UC). PTG-100 is orally stable because of its chemical and structural resistance to the acidic, reducing and proteolytic milieu of the gastrointestinal (GI) tract and was developed to have minimal systemic exposure and maximal GI tissue concentrations. Animal pharmacokinetic (PK) studies have shown that the drug is stable in the gut lumen and present in the colon, small intestine, mesenteric lymph nodes, Peyer's patches, and feces, but at very low concentrations in the blood (%F plasma < 0.5%) under normal and inflammatory conditions. In a dextran sulphate sodium (DSS)-induced colitis mouse model, PTG-100 induced a dose-dependent reduction in $\alpha4\beta7+$memory T cell homing to inflamed gut tissue and a significant improvement in mucosal damage with comparable activity to the mouse $\alpha4\beta7$ antagonist antibody DATK32. Fluorescence-activated cell sorter (FACS) analysis of whole blood from healthy cynomolgus monkeys demonstrated that blood receptor occupancy (RO) < 50% is correlated with efficacy in the mouse colitis studies. Following completion of IND-enabling studies, we conducted a phase 1 first-in-human study of orally-administered PTG-100 in normal healthy volunteers (NHVs) to assess safety/tolerability, PK and pharmacodynamic (PD) activity as measured by %RO and $\alpha4\beta7$ target expression (TE) on CD4+memory a4b7+T cells in peripheral blood.
**Aims & Methods:** We conducted a randomized, double-blinded, placebo-controlled phase 1 trial of single- (SAD) and multiple ascending dose (MAD) administration of PTG-100 in 70 male NHVs. MAD administration consisted of once daily dosing over 14 days. Subjects were monitored for safety / tolerability and underwent serial PK and PD evaluations.
**Results:** In the SAD portion of the study (n = 40), dose escalation proceeded to 1000 mg, the highest planned dose in the study. There were no serious adverse events or dose-limiting toxicities. All adverse events were of mild to moderate severity and resolved without complication. PTG-100 plasma levels were extremely low, but increased in a dose-dependent manner. There was a dose-dependent increase in blood RO of memory T cells, naïve T cells, and B cells with sustained RO beyond 24 hours following single dose exposure. Blood $\alpha4\beta7$ TE on memory T cells decreased in a dose-dependent manner consistent with internalization of the target with apparent plateauing at the 300 mg dose level. PTG-100 caused an increase in the percentage of circulating $\alpha4\beta7+$memory T cells, but not $\alpha4\beta7+$naïve T cells or $\alpha4\beta7+$B cells. MAD dosing is expected to be completed by mid-year 2016.
**Conclusion:** PTG-100 was well tolerated following single dose oral administration in NHVs with extremely low plasma exposure and evidence of target engagement and pharmacologic activity. As a novel orally-stable, GI-restricted and highly selective $\alpha4\beta7$ antagonist peptide therapeutic, PTG-100 may offer unique benefits compared to systemically administered biologics and non-specific immunomodulators. A Phase 2 study in UC patients is currently planned.
**Disclosure of Interest:** R. SHAMES: I am an employee of Protagonist Therapeutics.
L. TOZZI: I am an employee of Protagonist Therapeutics.
L. MATTHEAKIS: I am an employee of Protagonist Therapeutics.
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## P0299 IMPACT OF NON-MEDICAL SWITCHING OF ANTI-TUMOR NECROSIS FACTOR AGENTS ON HEALTHCARE COSTS IN EUROPE

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**Introduction:** Anti-tumor necrosis factor (anti-TNF) agents are an important treatment option for a variety of inflammatory diseases. Patients with a stable response to anti-TNF therapy may discontinue or switch treatments for non-medical reasons such as cost reduction. In the United States, non-medical switching (NMS) was demonstrated to be associated with increased healthcare resource utilization and cost.[1–3] The objective of this study is to estimate costs associated with NMS of anti-TNFs in a European setting.
**Aims & Methods:** We constructed a model to estimate costs associated with NMS from an originator anti-TNF to biosimilar infliximab among patients with Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriasis, and psoriatic arthritis in Denmark, The Netherlands, and Norway. Differences in resource utilization over 1 year due to NMS (i.e. comparing switchers to non-switchers) were estimated to be 7.12 outpatient visits, 0.02 inpatient admissions, 0.15 emergency department (ED) visits, and 1.16 additional anti-TNF infusions per patient [1, 2]. Cost inputs were based on data from the national healthcare authorities for each country, and included both disease-specific and all-cause medical (outpatient, inpatient, and ED visit) and drug (acquisition and administration) costs. Incremental costs attributable to NMS were summarized for each country in 2013/2014 currency. Costs were expressed in Euros.
**Results:** Average yearly costs were estimated to be €2, 349 (Denmark), €2, 730 (The Netherlands), and €4, 404 (Norway) per switcher. Increased costs were

**Abstract No: P0297**
**Table:** Key Safety Events Through 1 year of Follow-up.

| | CD | | PsA | | PsO | | Pooled Disease | |
|---|---|---|---|---|---|---|---|---|
| | PBO | UST[b] | PBO | UST | PBO | UST | PBO | UST |
| Pts treated/pt-yrs of F/u | 943/347 | 1749/1106 | 379/145 | 1018/850 | 733/182 | 3117/2566 | 2055/674 | 5884/4521 |
| Pts D/c due to AE(%) | 4.8 | 6.2 | 5.8 | 3.0 | 2.3 | 2.8 | 4.1 | 3.8 |
| Event rate per 100 pt-yrs AEs/SAEs | 712.2 /43.8 | 641.6/35.4 | 343.4/13.8 | 254.2/9.3 | 414.8/8.8 | 390.6/8.8 | 552.4/27.9 | 426.4 /15.4 |
| Infections/Serious infections[a] | 145.1 /6.9 | 134. /6.4 | 102.8 /0.7 | 78.0/0.9 | 120.7/1.7 | 137.4/1.4 | 129.4/4.2 | 125.4/2.5 |
| MACE | 0.00 | 0.09[c] | 0.69 | 0.71 | 0.55 | 0.55 | 0.30 | 0.46 |
| Deaths | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.19 | 0.00 | 0.11 |
| Malignancies (excl NMSC) | 0.00 | 0.36[d] | 0.00 | 0.12 | 0.55 | 0.43 | 0.15 | 0.35 |

[a]As assessed by investigator, [b] incl UST 1, 3, 4.5, or 6 mg/kg IV; UST 130 mg IV, UST SC 90 mg; [c]1 MACE: subarachnoid hemorrhage due to aneurysm rupture; [d]4 malignancies in 3 pts: 1 multiple myeloma, 1 adenocarcinoma & incidental carcinoid tumor; & 1 prostate cancer

driven primarily by costs for anti-TNF infusions (from 50% in Denmark to 75% in Norway to 90% in The Netherlands) (**Table**).

| | Incremental Costs Associated with NMS (in Euros) | | |
|---|---|---|---|
| | Denmark | Netherlands | Norway |
| Drug Infusions | 1, 188 (50.6%) | 2, 472 (90.5%) | 3, 338 (75.8%) |
| ED Visits | 11 (0.5%) | 27 (1.0%) | 0 (0%) |
| Inpatient Visits | 83 (3.5%) | 10 (0.4%) | 91 (2.1%) |
| Outpatient Visits | 1, 067 (45.4%) | 221 (8.1%) | 975 (22.1%) |
| TOTAL | 2, 349 (100%) | 2, 730 (100%) | 4, 404 (100%) |

**Conclusion:** Model results indicated that non-medical switching of anti-TNFs was associated with substantial additional costs in all three countries, driven primarily by the need for anti-TNF infusions.

**Disclosure of Interest:** T. Juday: I am an employee and shareholder in Abbvie Inc.
M. Skup: I am an employee and shareholder in Abbvie Inc.
C. Streuper: I am an employee of Abbvie Inc.
U. Moerch: I am an employee of Abbvie Inc.
G.S. Kopperud: I am an employee of Abbvie Inc.
O. Henriksen: I am an employee of Abbvie Inc.
S. Johnson: MedicusEconomics received payment from Abbvie Inc. for the conduct of this study.
T. O'Connell: Medicus Economics received payment from Abbvie Inc. for the conduct of this study.

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### P0300 COMPARATIVE ANALYSIS OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND IRON DEFICIENCY/ ANAEMIA TREATED WITH ORAL VERSUS INTRAVENOUS IRON - A RETROSPECTIVE CLAIMS DATA ANALYSIS TO ASSESS THE IMPACT ON HOSPITALISATION IN GERMANY

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**Introduction:** Patients with Inflammatory Bowel Disease (IBD) are likely to have iron deficiency with an estimated prevalence of 60–80%, whereas anaemia manifests in about one-third of patients. Iron deficiency can have a significant impact on a patient's quality of life. Intravenous iron and oral iron are indicated for patients with IBD and iron deficiency or iron deficiency anaemia.

**Aims & Methods:** The aim of this study was to compare patients with IBD and Iron Deficiency/Anaemia (ID/A) newly treated with oral or intravenous iron regarding the impact on hospitalisation in Germany. Pooled claims data from the Health Risk Institute research database were used which comprises data from 75 German health insurances on an anonymised individual level. IBD patients with ID/A were identified by ICD-10-GM codes in 2013. Type of incident iron treatment, oral/intravenous iron, were assessed via ATC codes. All patients had to be insured continuously during the individual pre-observation period of 4 quarters for the incidence assessment of iron treatment. A 1:1 propensity score matching was performed to compare patients with oral iron to patients with intravenous iron using age, gender, and the updated Charlson Comorbidity Index. Matching couples were identified applying the nearest neighbor matching and a caliper of 0.05 was used. Outcome measures focused on impact on hospitalisation. P-values were calculated applying the McNemar's test and the Wilcoxon signed rank test.

**Results:** In total, 2, 379 IBD patients had ID/A, of which 589 received oral iron treatment for the first time, 442 patients were newly treated with intravenous iron, whereas 1, 348 patients received no iron treatment in 2013. After matching oral vs. intravenous iron, 380 IBD patients remained in each treatment cohort. Mean age was balanced to 42.3 and 42.2 years for oral and intravenous iron patients and 67% vs. 61% were female, respectively. Insurance status (member, family insured, pensioner) were equally distributed in the matched cohorts. All-cause hospitalisations were reported in 48% of the oral iron patients vs. 37% of the intravenous iron patients ($p = 0.001$), and ID/A-related hospitalisations in 14% and 5%, respectively ($p < 0.001$). Mean duration of ID/A-related hospitalisations was significantly shorter for patients treated with intravenous iron (9.6 vs. 7.0 days; $p < 0.001$).

**Conclusion:** Real-world evidence suggests that IBD patients with ID/A treated with intravenous iron had fewer all-cause and ID/A-related hospitalisations, and had a shorter duration of ID/A-related hospitalisation vs. IBD patients with ID/A treated with oral iron. Further research is warranted to assess the long-term effects of iron supplement treatment.

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T. Hardt: Thomas Hardt is employed by Vifor Pharma Deutschland GmbH, Munich, Germany.
J. Haas: Jennifer Haas is employed by Xcenda GmbH (Hannover, Germany), a company that received funding from the Vifor group of companies to conduct the analysis described herein and for preparation of the abstract.
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### P0301 IMMUNOGENICITY PROFILE AND PREDICTORS OF TLS AND ADA DEVELOPMENT OF BIOSIMILAR INFLIXIMAB DURING THE FIRST 6 MONTHS OF THE THERAPY: RESULTS FROM A PROSPECTIVE NATIONWIDE COHORT

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**Introduction:** Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product and its use is mandatory in all anti-TNF-naïve IBD patients in Hungary since May 2014.

**Aims & Methods:** In the present study we aimed to prospectively evaluate the immunogenicity profile of the biosimilar infliximab and predictors of TDM in IBD in a nationwide, multicentre cohort. Demographic data were collected and a harmonized monitoring strategy was applied. Clinical and biochemical activity were evaluated at weeks 14, 30 and 54. Routine therapeutic drug monitoring (TDM) was applied. Trough level (TL) and anti-drug antibody (ADA) concentration were measured by ELISA (LT-005, Theradiag, France) at baseline and at 2, 6, 14, 30 and 54 weeks right before anti-TNF administration during the induction treatment.

**Results:** 291 consecutive IBD patients (184 CD patients and 107 UC patients) were included in the present cohort. 24.5% of CD patients and 14% of UC patients had received previous anti-TNF therapy. None of the patients had received infliximab within 12 months prior to initiation of the biosimilar infliximab. 60/52% of CD/UC patients received concomitant immunosuppressives at baseline. Mean TLs were 20.1, 14.7, 5.1 and 3.9 $\mu$g/ml at weeks 2, 6, 14 and 30. Early TLs were higher in CD compared to UC at weeks 2 (19.1 vs 15.1 $\mu$g/ml, $p = 0.05$) and 6 (16.7 vs. 12.1 $\mu$g/ml, $p = 0.046$) with no significant differences in TLs thereafter at week 14 and 30. ADA positivity rates were 3.8%, 16.1%, and 24.1% in naïve patients at weeks 0, 14, and 30 ($n_{total} = 229$, 192 and 143). TLs were lower at week 2 and 6 ($p = 0.02$ and $p = 0.005$), but not week 14 or 30 in patients with previous anti-TNF exposure, compared to naïve patients, coupled with higher ADA positivity. Concomitant IS use prevented early ADA formation in anti-TNF naïve patients (24.6% vs 11.2%, $p = 0.03$) by week 14, but the effect was lost by week 30 (29.8% and 21.2%, p = ns). 21 (7.2%) patients had infusion reactions during induction or maintenance treatment, of which 13 patients had received previous infliximab treatment.

**Conclusion:** Drug TLs and ADAs in IBD patients at weeks 0, 2, 14 and 30 weeks were in line with results reported for the originator in previous studies. Early TLs were slightly lower in UC compared to CD. Patients with previous exposure to anti-TNFs had lower early TL coupled with ADA positivity and were more likely

to develop infusion reactions. Concomitant IS use prevented early but not later ADA development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0302 RATE AND PREDICTORS OF MUCOSAL HEALING IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH THIOPURINES: RESULTS OF A MULTICENTRIC COHORT STUDY

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**Introduction:** Mucosal healing (MH) has become the optimal treatment goal in ulcerative colitis (UC) as it is associated with a better outcome. Thiopurines are immunosuppressants currently used in UC. However, MH rate is little known in UC patients treated with thiopurines. Our study aimed to assess rate and predictors of MH in UC patients treated with thiopurine monotherapy.
**Aims & Methods:** Patients were selected from prospective and administrative databases of 5 hospitals. Inclusion criteria were: UC, thiopurine monotherapy longer than 6 months and endoscopic evaluation before (T0) and at least 6 months after treatment initiation (T1). Exclusion criteria were: history of anti-TNF alpha, methotrexate or ciclosporin intake. Baseline characteristics of the patients (age at diagnosis, Montreal classification, complications) were collected in a standardized anonymous questionnaire (File Maker Pro v.12®). Clinical (Mayo score), biology and endoscopic (Mayo score, UCEIS) data were collected at T0, T1 and at latest news (T2). MH definition was: Mayo endoscopic score $\leq 1$ or UCEIS $\leq 2$. Patients with and without MH were compared by Mann Whitney-Wilcoxon test for non-parametric quantitative variables and by Student test for parametric variables.
**Results:** Out of 902 UC patients, 125 received at least 6 months of thiopurine monotherapy: 45 were excluded because previous ciclosporin treatment for acute severe colitis (N = 9) or lack of endoscopic evaluation (N = 36). Overall 80 patients (31 women) aged 43 (32–58), were included. Median UC duration was 10.5 (6–16) years. UC extent was E1, E2 and E3 in 8 (10%), 33 (42.5%) and 37 (47.5%) respectively. At T0, full Mayo score, endoscopic Mayo score and UCEIS were 8 (6.75–10), 3 (2–3) and 5 (3–6) respectively. At T1, after a mean of $38 \pm 31.3$ months, full Mayo score, endoscopic Mayo score, UCEIS were 3.5 (1–6), 2 (0–2.25) and 2 (0–4) respectively. Clinical remission was achieved in 62.7%, MH in 43.7% and histologic healing in 38%. Independent predictive factors of MH were: thiopurine exposure $\geq 2$ years [OR (CI95%) = 2.9 (1.1–7.6); p = 0.03] and acute severe colitis prior to thiopurine [OR (CI95%) = 5.9 (1.1–32); p = 0.04]. At T1, rectal bleeding Mayo sub-score $\leq 1$, BMI $\geq 25$ kg/m$^2$ and mean corpuscular volume (MCV) $\geq 95$ fL had a negative predictive value of 100%, 75% and 73% respectively. At T2 (N = 49), after a median of 5.9 (3.4–9.5) years follow up, 79% achieved clinical remission and 63.2% MH. Eighty percent who achieved MH at T1 had MH at T2.
**Conclusion:** This study shows that thiopurine monotherapy in UC is associated with MH in 43.7%. Independent predictive factors of MH are exposure to thiopurine $\geq 2$ years and severe acute colitis prior to thiopurine. Absence of rectal bleeding, BMI $\geq 25$ kg/m$^2$ and MCV $\geq 95$fL have good predictive value for MH.
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A. Amiot: Advisory board: Takeda, Abbvie, Gilead Consulting: Abbvie, Biocodex, Travel accomodation: Biocodex, Abbvie, MSD Lectures: Abbive, Takeda, MSD, Ferring.
S. Chaussade: Mayoli Fujifilm Given Imaging MauneaKea.
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All other authors have declared no conflicts of interest.

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## P0303 EFFICACY AND SAFETY OF TNF ANTAGONIST FOR THE TREATMENT OF INTERNAL FISTULIZING CROHN'S DISEASE

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**Introduction:** Anti-TNF$\alpha$ (Tumour necrosis factor $\alpha$) changed the way of treating Crohn's disease, including in case of fistulizing disease. To date, studies assessing the efficacy of anti-TNF$\alpha$ treatment in fistulizing CD mainly focused on perianal fistulae. Data assessing their use in case of internal fistulae are lacking. Intestinal resection is often preferred, considering the high risk of abscess for non-drained fistulae. The aim of the present study was to assess the efficacy of anti-TNF$\alpha$ treatment in a large cohort of CD patients complicated with internal fistula (excluding entero-cutaneous and perianal fistulae).
**Aims & Methods:** This was a multi-centric observational retrospective study. All CD patients who started anti-TNF$\alpha$ treatment for internal fistula were included. The primary outcome was the occurrence of intestinal resection. The secondary outcomes were the occurrence of internal fistula healing following anti-TNF$\alpha$ treatment, and the safety profile of anti-TNF$\alpha$.
**Results:** One hundred and seven (107) patients were included. After a median follow-up of 3.5 [1.6–5.6] years, 52 patients (48.6%) underwent a major abdominal surgery. Indications for surgery were the absence of fistula healing for 32 patients (61.5%), occlusion or sub-occlusion resulting from concomitant stenosis for 15 patients (28.8%), intestinal adenocarcinoma for 3 patients (5.7%), peritonitis secondary to intestinal perforation for 2 patients (3.8%). Cumulative probabilities for being free from surgery were 67%, 58% and 51% at 1, 3 and 5 years respectively. The complex characteristic of fistula (HR 3.49; 1.33 to 11.2; p = 0.01), C-reactive protein (CRP) > 18 mg/L (HR 3.63; 1.52 to 9.72; p = 0.003) and albumin < 30 g/L (HR 3.37; 1.46 to 7.70; p = 0.005) were associated with surgery. Fistula healing was obtained for 41% of patients (n = 44) with a mean duration of 12.5 [5.7 – 22.8] months. The cumulative probabilities of sustained fistula-healing were 20%, 35% and 47% at 1, 3 and 5 years after anti-TNF$\alpha$ treatment started. Only albumin $\geq 35$ g/L (HR 6.21; 2.53 to 16.73; p < 0.0001) was significantly and independently associated to fistula healing. Septic complications concerned 15 patients (14.0%), 11 patients (10.3%) developed an abscess. Four patients (3.8%) developed malignancy. Four patients (3.8%) died, 3 patients from an intestinal adenocarcinoma at 10 months, 5 et 7 years from anti-TNF$\alpha$ start; and 1 patient from a septic-shock at 3 months from anti-TNF$\alpha$ introduction.
**Conclusion:** Anti-TNF$\alpha$ treatment is useful for half of CD patients complicated with internal fistula, which has to be balanced against significant septic and malignant risks. Their use should be proposed to a selected population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0304 DIFFERENT INDUCTION RESPONSE CRITERIA DO NOT INFLUENCE 1 YEAR RESPONSE AND REMISSION RATES OF USTEKINUMAB 90 MG Q8W IN PHASE III PROGRAM

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**Introduction:** Crohn's disease Phase III maintenance clinical trials with biologics are typically randomized withdrawal trials, in which patients that responded after induction with a specific biologic are re-randomized to either maintenance therapy or placebo. Different response criteria have been used to qualify responders for these studies, such as CDAI 70 at week 2, 4 or 6 and CDAI 100 at week 8, but the influence of this criterion on remission results at year 1 has not been investigated. In the IM-UNITI study, patients with a CDAI 100 response 8 weeks after ustekinumab induction were re-randomized to either placebo, ustekinumab 90 mg Q12w or ustekinumab 90 mg Q8w (every 8 weeks). Non-responders to ustekinumab induction, as well as patients that received placebo for induction remained blinded in the trial. Non-responders to ustekinumab induction received ustekinumab 90 mg SC Q8w at week 0 of IM-UNITI. As a result, since both ustekinumab CDAI-100 responders and non-responders received 90 mg Q8w, remission rates at 52 weeks of total treatment can be calculated for ustekinumab 90 mg Q8w for patients with different induction response criteria.
**Aims & Methods:** Pre-specified analyses were conducted to evaluate the proportion of patients in remission and CDAI-100 response at 52 weeks of total treatment in the different arms of IM-UNITI for patients with a - 70 point CDAI response to ustekinumab at week 6 of induction. - 70 point CDAI response to ustekinumab at week 3 of induction - 100 point CDAI response to ustekinumab at week 8 of induction (original response criterion). Subsequently, the overall proportion of remitters and CDAI-100 responders at week 52 of total treatment was calculated for patients with a CDAI-70 response to ustekinumab respectively at week 3 or 6 of induction taking into account their relative distribution over the randomized or non-randomized arms receiving 90 mg Q8W.
**Results:** Remission rates after 52 weeks of total treatment in patients receiving 90 mg ustekinumab Q8w are summarized below.

**Abstract No: P0304**

| Response criterion | Randomized group (CDAI-100 responders at week 8) #patient randomized | Week 52 remission rate in 90 mg Q8w arm | Non-randomized group (no CDAI-100 at week 8) #patients at start of maintenance | Week 52 remission rate (90 mg Q8w) | Overall week 52 remission rate in responders |
|---|---|---|---|---|---|
| **CDAI 70 responder week 6** | **347** | **55.0%** | 127 | 42.5% | **51.7%** |
| **CDAI 70 responder week 3** | **283** | **60.7%** | 102 | 41.2% | **55.5%** |
| **CDAI 100 responder week 8 (original response criterion)** | 388 | 53.1% | | | **53.1%** |

Similarly, CDAI-100 response rates after 52 weeks of total treatment in patients receiving 90 mg ustekinumab Q8w were calculated for the different induction response categories. Rates were 60.8%, 58.3%, and 59.4% for CDAI-70 responders at week 3, 6, and CDAI-100 responders at week 8 respectively.
**Conclusion:** The majority of patients with CDAI-70 response at either week 3 or 6 after induction also had a CDAI-100 response at week 8. Using different qualifiers for response to ustekinumab induction did not result in different response or remission rates after 1 year of treatment in patients treated with ustekinumab 90 mg Q8w.
**Disclosure of Interest:** D. Naessens: Employee of Janssen Pharmaceutica NV.
J. Johanns: Employee of Janssen Research and Development, LLC.
C. Gasink: Employee of Janssen Research and Development, LLC.

## P0305 PREDICTING OF SHORT AND MEDIUM-TERM EFFICACY OF BIOSIMILAR INFLIXIMAB THERAPY. DO TROUGH LEVELS/ ADAS OR CLINICAL/BIOCHEMICAL MARKERS PLAY A MORE IMPORTANT ROLE?

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**Introduction:** Biosimilar infliximab CT-P13 received EMA approval in June 2013 for all indications of the originator product and its use is mandatory in all anti-TNF naïve IBD patients in Hungary since May 2014.
**Aims & Methods:** In the present study we aimed to prospectively evaluate the predictors of short and medium-term clinical outcome in patients treated with the biosimilar infliximab in two IBD centers in Hungary. Demographic data were collected and a harmonized monitoring strategy was applied. Clinical and biochemical activity were evaluated at weeks 14, 30 and 54. Therapeutic drug monitoring (TDM) was regularly used. Trough level (TL) and anti-drug antibody (ADA) concentration were measured by ELISA (LT-005, Theradiag, France) at baseline at 14, 30 and 54 weeks and in the above 2 centers at weeks 2 and 6 right before anti-TNF administration during the induction treatment.
**Results:** 291 consecutive IBD patients (184 CD patients and 107 UC patients) were included in the present cohort. 24.5/14% and 62/52% of CD and UC patients received previous anti-TNF and concomitant immunosuppressives at baseline therapy. Mean TLs were 20.1, 14.7 and 5.1 $\mu$g/ml at weeks 2, 6 and 14 (n = 124, 86 and 158). Cumulative ADA positivity rates were 8.7%, 19.3%, and 28.0% in IBD patients at weeks 0, 14, and 30 ($n_{total}$ = 229, 192 and 143). Early TLs at week 2 were predicting short term- (week 14 response/remission, $AUC_{TLweek2}$ = 0.715/0.721, p = 0.05/0.005,) but not medium-term (week 30 or 54) clinical efficacy. TLs measured at week 6/14 were not predicting either short or medium-term clinical outcome. In addition, early ADA status by week 14 (p = 0.04–0.05, OR: 2.1–2.6 for week 14 and 30), early clinical response ($p < 0.001$, OR: 7.7–42.8 for week 30/54) and normal CRP at week 14 (p = 0.005–0.0001, OR: 3.2–7.8 for week 14 and 30) and previous anti-TNF exposure (p = 0.03–0.0001, OR: 2.22–6.25, for week 14, 30 and 54) were associated with short and medium-term clinical outcomes (response and remission).
**Conclusion:** Early TLs were only associated with short-term clinical outcomes, while ADA development by week 14, early clinical response and normal CRP at week 14 and previous anti-TNF exposure were predicting medium-term clinical outcomes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0306 TOFACITINIB FOR INDUCTION THERAPY IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS IN TWO PHASE 3 CLINICAL TRIALS: RESULTS BY LOCAL AND CENTRAL ENDOSCOPIC ASSESSMENTS

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**Introduction:** Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). Two Phase 3 randomised placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951) demonstrated efficacy of tofacitinib 10 mg twice daily (BID) vs placebo as induction therapy for patients with moderately to severely active UC.[1].
**Aims & Methods:** We describe here the clinical efficacy endpoints assessed by local endoscopy readings along with the previously reported results assessed by central readings. Patients in OCTAVE Induction 1 and 2 were randomised (4:1) to receive treatment with tofacitinib 10 mg BID or placebo for up to 9 weeks (wks). Patients were ≥18 years old with moderately to severely active UC (baseline Mayo score ≥6, rectal bleeding subscore ≥1 and endoscopic subscore ≥2). Patient eligibility was assessed based on central endoscopic reading. Patients had previous failure or intolerance to treatment with ≥1 of corticosteroids, thiopurines, or tumour necrosis factor inhibitors. The following efficacy endpoints were assessed at Wk 8: mucosal healing (defined as Mayo endoscopic subscore ≤1), remission (study primary endpoint, defined as Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0) and clinical response (decrease from baseline Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1). Clinical outcomes were measured using both local (ie site) and central endoscopic readings at baseline and Wk 8.
**Results:** At Wk 8, significantly more patients receiving tofacitinib 10 mg BID achieved mucosal healing in both studies vs placebo as demonstrated by both central and local endoscopic readings (Table). Similar results were observed with remission and clinical response at Wk 8. The observed rates as well as the magnitude of treatment differences based on local endoscopic reading were generally higher than those assessed by central reading. There was good agreement between locally and centrally read endoscopic subscores (kappa = 0.63 (95% CI 0.58, 0.67) and 0.62 (95% CI 0.57, 0.67) in OCTAVE Induction 1 and 2, respectively).
**Conclusion:** In patients with moderately to severely active UC, who were qualified for both Phase 3 studies on central reading, treatment effects observed with local endoscopic readings were similar or slightly higher and, overall, consistent with central readings. Both methods demonstrated the significant effect of tofacitinib vs placebo for induction therapy.
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**Table:** Summary of efficacy endpoints at Wk 8 determined by local and central reading.

| | OCTAVE Induction 1 | | | OCTAVE Induction 2 | | |
|---|---|---|---|---|---|---|
| | Tofacitinib 10 mg BID N = 476 | Placebo N = 122 | Difference (95% CI) | Tofacitinib 10 mg BID N = 429 | Placebo N = 112 | Difference (95% CI) |
| **Mucosal healing, n (%)** | | | | | | |
| Central read | 149 (31.3)*** | 19 (15.6) | 15.7 (8.1, 23.4) | 122 (28.4)*** | 13 (11.6) | 16.8 (9.5, 24.1) |
| Local read | 202 (42.4)*** | 28 (23.0) | 19.5 (10.8, 28.2) | 156 (36.4)*** | 17 (15.2) | 21.2 (13.1, 29.2) |
| Difference local vs central read | - | - | 3.8 | - | - | 4.4 |
| **Remission, n (%)** | | | | | | |
| Central read | 88 (18.5)** | 10 (8.2) | 10.3 (4.3, 16.3) | 71 (16.6)*** | 4 (3.6) | 13.0 (8.1, 17.9) |
| Local read | 118 (24.8)** | 14 (11.5) | 13.3 (6.5, 20.2) | 89 (20.7)*** | 6 (5.4) | 15.4 (9.7, 21.1) |
| Difference local vs central read | - | - | 3.0 | - | - | 2.4 |
| **Clinical response, n (%)** | | | | | | |
| Central read | 285 (59.9)*** | 40 (32.8) | 27.1 (17.7, 36.5) | 236 (55.0)*** | 32 (28.6) | 26.4 (16.8, 36.0) |
| Local read | 289 (60.7)*** | 42 (34.4) | 26.3 (16.8, 35.8) | 249 (58.0)*** | 33 (29.5) | 28.6 (18.9, 38.2) |
| Difference local vs central read | - | - | −0.8 | - | - | 2.2 |

Full analysis set, non-responder imputation. **$p < 0.01$; ***$p < 0.001$ vs placebo, based on the Cochran-Mantel-Haenszel chi-squared test stratified by prior treatment with tumour necrosis factor inhibitors, corticosteroid use at baseline and geographic region. BID, twice daily; CI, confidence interval; Wk, week.

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All other authors have declared no conflicts of interest.

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### P0307 ESCHERICHIA COLI NISSLE 1917 MODULATE GUT MICROBIOTA COMPOSITION IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** *Escherichia coli* Nissle (ECN) 1917 is a Gram-negative bacteria that belongs to the family of Enterobacteriaceae, and it is currently used as probiotic drug in the management of infectious gastroenteritis and in maintenance of remission in ulcerative colitis (UC) patients. ECN has been described to act also on intestinal epithelial barrier but few information exists on the influence of this probiotic on the gut microbiota composition.

**Aims & Methods:** The aim of our study was to evaluate the effect of administration of ECN in the qualitative and quantitative composition of the intestinal bacterial flora. Five patients affected by UC were treated with ECN (1 pill daily) for 10 days follwed by 2 pills per day for further 20 days. Fecal samples were collected before starting the treatment (T0), after 10 days from the beginning of the therapy (T1) and one month following the start of treatment (T2). Genomic DNA was isolated from the entire set of samples. The V1-V3 region of 16 S rRNA locus was amplified on a 454-Junior Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v.1.8.0), grouped into operational taxonomic units (OTUs) by sequence matching against Greengenes database. The $\alpha$ and $\beta$ diversity and the Kruskal Wallis test were performed by QIIME software.

**Results:** The T test on good's coverage index (measure of total number of species represented in a sample) revealed that the qualitative composition of the gut microbiota between the T0 and T2 conditions resulted significantly different. Box plot of Shannon and Chao I indices revealed an increase in the median index values at the time point T1, which means an increase in the OTU total number at T1. This indicates an increase of the microbiota wellness at this time point. Post hoc analysis at phylum taxonomic level, revealed that Firmicutes relative abundance in the condition T0 versus T1 resulted significantly different, with a decrease of Firmicutes at T1. Indeed, at family taxonomic level the post hoc analysis revealed that Clostridiaceae relative abundance in the condition T0 versus T1, and also in T1 versus T2, differed significantly, with a T1 median value higher than the T0 and T2 values. At genus level, the T test confirms the variability in the two conditions (T0 and T2), with significantly differences for *Actinomyces*, *Anaerostipes*, *Bacteroides*, *Bulleidia*, *Corynebacterium*, *Dialister*, *Enterobacteriaceae*, *Erysipelotrichaceae*, *Finegoldia*, *Granulicatella*, *Lactobacillaceae*, *Peptoniphilus*, *Phascolarctobacterium*, *Roseburia*, *Serratia*, *Veillonellaceae*, *Veillonella_dispar*, *belonging to Firmicutes*, *Bacteroidetes* and *Proteobacteria phyla*.

**Conclusion:** Our data show that treatment with ECN leads to an improvement of the qualitative composition of the gut microbiota in patients affected by UC. These effects are stronger at the end of treatment in terms of wealth, with a stable variability between the genera after 1 month of treatment. Further studies should be performed to investigate the effect of this gut microbiota modulation on the history of the disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0308 THE INCIDENCE OF AND TIME TO SUBOPTIMAL THERAPY AMONG PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE INITIATING TUMOUR NECROSIS FACTOR ANTAGONISTS: A MULTI-COUNTRY CHART REVIEW

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**Introduction:** Tumour necrosis factor antagonists (anti-TNF) have proven efficacy in Crohn's disease (CD) and Ulcerative Colitis (UC) patients, although many of them require therapy changes over time to maintain clinical benefit. Treatment modifications (i.e., dose escalation, switch to another anti-TNF, surgery, or addition of other medications) can be used as surrogate indicators of loss of response and may be considered as markers of suboptimal therapy.

**Aims & Methods:** The aim of this study was to quantify the incidence of and time to suboptimal therapy among adult patients with UC and CD using real-world clinical practices. A retrospective chart review study conducted in six countries (Canada, France, Germany, Italy, UK, and Spain) recruited CD and UC patients initiating infliximab or adalimumab between June 2009–2013 (index therapy). Indicators of suboptimal therapy were anti-TNF dose escalation (assessed >4 months after index to allow for initial dose optimizations), augmentation with aminosalicylates, immunomodulators, or corticosteroids, discontinuation of initial anti-TNF, switching to another anti-TNF, or disease-related surgery. Time to the first occurrence of the indicator of suboptimal therapy was measured using the Kaplan-Meier Method where patients were censored after discontinuation and at the end of the follow-up period.

**Results:** 657 CD (mean age of 39.2 years, 51% female) and 538 UC (mean age of 41.6 years, 47% female) patients initiating anti-TNF therapy were included. Among the CD cohort, 55.6% and 44.4% were initiated therapy with infliximab and adalimumab, respectively, whereas 92.2% of UC patients had been initiated

therapy with infliximab. Mean disease duration was longer for CD patients compared to UC [8.8 (SD = 8.6) vs. 7.1 (SD = 7.2) years]. A higher proportion of UC patients had at least one non-biologic treatment at index compared to CD patients (83.6% vs. 70.6%). Median time to at least one indicator of suboptimal therapy was 12.5 (95% CI: 10.5–15.2) and 17.5 (95% CI: 15.3–21.1) months for UC and CD patients, respectively. Within the first 12 months, the probability of discontinuation was highest indicator of suboptimal therapy (0.23 and 0.21 for UC and CD, respectively) followed by dose escalation (0.21 and 0.14 for UC and CD, respectively).
**Conclusion:** In this large multi-national cohort, the majority of patients initiating anti-TNF therapy had at least one indicator of suboptimal therapy within the first 12 months for UC and 17 months for CD. The most common indicators of suboptimal therapy were dose escalation and discontinuation with anti-TNF therapies. Future research should assess the potential for alternative therapies to improve treatment response rates among patients initiating anti-TNF therapies.
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J. Lindsay: Grant/research support and is on speaker bureau with: MSD, Abbvie, Hospira, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Vifor Pharma, Atlantic Health care, Actavis (Warner Chilcott), and Tillotts.
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J.P. Gisbert: Grant/research support from and is on speaker bureau with MSD, Abbvie, Hospira, Kern Pharma, Takeda, Janssen, Pfizer, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka Pharmaceutical, Vifor Pharma.
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## P0309 TREATMENT WITH EUDRAGIT-COATED MESALAZINE TABLETS SIGNIFICANTLY IMPROVES THE WORK PRODUCTIVITY IN PATIENTS WITH MILDLY TO MODERATELY ACTIVE ULCERATIVE COLITIS

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**Introduction:** Patients with active ulcerative colitis (UC) experience several symptoms that affect and reduce their work productivity.
**Aims & Methods:** The aim of this study was to assess the impact of an 8–week treatment with 3 g/day Eudragit-coated mesalazine tablets on the work productivity in patients with mild to moderate UC measured by the WPAI:UC. Data were collected from a phase III, multi-centre, double-blind, double-dummy study with mildly to moderately active UC patients receiving either the novel high-dose TID 1000 mg mesalazine tablet or the registered TID 2 × 500 mg mesalazine tablet Salofalk® for 8 weeks (SAT-25/UCA trial). The WPAI:UC is a self-report questionnaire measuring on 4 different scales the impairment of work and other activities due to symptoms of UC: 1) absenteeism (work time missed), 2) presenteeism (impairment while working), 3) overall work productivity loss (combined absenteeism and presenteeism) and 4) activity impairment (limitations of non-work activities) during the previous 7 days. During the 8-week treatment phase patients completed the WPAI:UC every other week. Clinical disease activity was measured using the Clinical Activity Index (CAI).
**Results:** Of the 306 randomised patients, only those with an impairment in WPAI:UC at baseline were used for analysis (n = 297, 97%). For absenteeism, presenteeism and overall work productivity loss only employed patients (n = 186, 61%) at baseline were evaluated. 43% of the employed patients achieved clinical remission at week 8. 89%, 74%, 76% and 76% of these patients showed an improvement in absenteeism, presenteeism, overall work productivity and activity impairment at week 8, respectively. In all four scales of the WPAI:UC, an 8-week mesalazine treatment significantly reduced impairment of work productivity ($p < 0.0001$). These changes correlated with an improvement of the clinical activity (defined as CAI improvement $\geq 3$ points) ($p < 0.0001$), except for absenteeism. Patients achieving clinical remission at week 8 (defined as CAI $\leq 4$ with normalization of stool frequency and absence of rectal bleeding at week 8) were significantly less affected in their work productivity compared to patients not achieving clinical remission ($p < 0.0001$), except for absenteeism. No statistically significant differences for all scales of the WPAI:UC were observed between the two different mesalazine formulations.
**Conclusion:** This large study demonstrates that an 8-week treatment with 3 g/day Eudragit-coated mesalazine tablets in patients with active UC leads to significant improvements in work productivity. At week 8, patients in clinical remission are significantly less affected in their work productivity than patients being not in clinical remission. Improvement of clinical activity correlates with significant improvement of work productivity as assessed with the WPAI:UC.
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T. Nacak: Employee of Dr. Falk Pharma GmbH.
R. Greinwald: Employee of Dr. Falk Pharma GmbH.
All other authors have declared no conflicts of interest.

## P0310 EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB FOR THE INDUCTION OF REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS

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**Introduction:** Vedolizumab has been approved for the treatment of both Crohn's disease (CD) and ulcerative colitis (UC). However, data of the effectiveness and safety of this drug in clinical practice are scarce.
**Aims & Methods:** Aims: 1) To assess the short-term effectiveness of vedolizumab in inflammatory bowel disease (IBD) patients; 2) To identify factors associated with the response to the treatment; and 3) To evaluate the safety of this drug in clinical practice. Methods: Observational, multicenter, nationwide study. Patients treated with vedolizumab due to active IBD (UC, Partial Mayo Score $\geq 2$; CD, Harvey-Bradshaw $> 4$) were retrospectively included. Short-term response was evaluated at week 14. The variables associated with the short-term effectiveness were identified by logistic regression analysis. Adverse events during the treatment were recorded.
**Results:** Ninety-five patients were included. Mean age was 44 years (standard deviation [SD] = 14 years), mean time of evolution of the disease was 11 years (SD = 7 years), 57% were female, and 30% were current smokers. Fifty-three patients (56%) were diagnosed with CD and 42 (44%) with UC. Among CD patients, 57% had ileocolonic involvement, and 25% ileal location; 60% had inflammatory behaviour, 28% fistulizing disease, and 32% perianal disease. Among UC patients, 50% had left-sided colitis, and 47% extensive colitis. 42% suffered extraintestinal manifestations, and 34% had been operated on due to IBD: 22 patients (22%) had undergone intestinal resection and 10 patients (10.5%) had undergone surgery due to perianal disease. With respect to previous treatments, 93% patients had received azathioprine, 29% mercaptopurine, 36% methotrexate and 10% cyclosporine. Eighty-nine patients (94%) had been

refractory to biologic agents before starting vedolizumab: 5 patients (5%) had previously failed to 4 biologic agents, 26 (27%) to 3, 46 (48%) to 2, and 12 (6%) to 1 biologic agent. Overall, 40% of the patients were under concomitant immunosuppressants when they were started on vedolizumab. After the induction doses (week 14th), 75% (95%CI, 65–83%) of patients responded to the treatment (23% achieved remission and 52% partial response). The percentages of remission and response were similar between CD and UC patients: 19 vs. 30% ($p = 0.2$) for remission, and 73 vs. 75% ($p = 0.8$) for response. We could not identify any factor associated with response to vedolizumab (including the type of IBD and concomitant immunomodulators). Nine patients (9.5%) had adverse events during the treatment, all of them being mild: 2 respiratory infection, 2 dizziness, 1 fatigue, 1 herpes infection, 1 palmar erythema, 1 arthralgia and 1 infusion reaction.

**Conclusion:** In the short-term, vedolizumab seems to be effective and safe for the treatment of IBD (both CD and UC), even in refractory patients.

**Disclosure of Interest:** J.P. Gisbert: Served as a speaker, a consultant and advisory member for or has received research funding from MSD, Abbvie, Hospira, Kern Pharma, Takeda, Janssen, Pfizer, Ferring, Faes Farma, Shire, Dr Falk Pharma, Chiesi, Casen Fleet, Gebro Pharma, Otsuka, Vifor Pharma.
All other authors have declared no conflicts of interest.

## P0311 EFFICACY OF EXCLUSIVE ENTERAL NUTRITION IN ADULT ACTIVE CROHN'S DISEASE WITH COMPLICATIONS OR FAILURE OF MEDICAL TREATMENT

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**Introduction:** Complicated active Crohn's disease (CD) patients may not need emergent surgery or not be suitable for surgery due to malnutrition. They may also not be appropriate for corticosteroids or biologics due to stricture, intestinal fistula and/or abdominal abscess. Some patients had poor response to medical therapy. We aim to investigate the efficacy of EEN in induction of remission in active CD patients with complications or poor response to drugs.

**Aims & Methods:** Active CD patients who had been diagnosed as complicated with stricture, intestinal fistula, abdominal abscess and no response to drugs, were recruited since July 2013 to October 2015. Patients were offered EEN for 12weeks without other drugs except patients with abscess could use antibiotic therapy with or without percutaneous drainage. Demographics and clinical variables were recorded.

**Results:** 48 patients aged 18–60 with CD were finally involved. 10 patients diagnosed as refractory CD; 10 accompanied with stenosis and 33 with intestinal fistula (4 enterocutaneous fistulas and 25 intra-abdominal abscesses). After 12 weeks EEN, the CDAI decreased obviously ($213.7 \pm 62.7$ VS $94.8 \pm 41.6$, $P = 0.000$). 4 patients only achieved partial remission, while 3 of them insisted to continue EEN except 1 patient transferred to surgery. Among patients with enterocutaneous fistula, 3 (3/4, 75%) got fistula closure after EEN. In patients with stenosis, 2/10 (20%) had no response to EEN and were transferred to surgery. 2/10 (20%) had partial remission and 6/10 (60%) achieved completely clinical remission after 12 weeks EEN. 10 (10/10, 100%) refractory CD patients all achieved clinical remission. 19 patients complicated with intra-abdominal abscess got abscess disappeared (19/25, 76%). 23 patients performed colonoscopy before and after EEN, 7 patients (7/23, 30.4%) reached mucosal healing. The inflammatory index of patients was significantly decreased (hs-CRP: $9.17 \pm 4.02$ mg/l VS $3.33 \pm 3.15$, $p = 0.00$; PLT: $321.42 \pm 105.5$*10E9/l VS $241.42 \pm 55.75$*10E9/l, $p = 0.00$). The nutritional parameters such as BMI were increased obviously ($17.09 \pm 2.26$ VS $18.41 \pm 1.93$, 0.06) and the NRS 2002 score decreased significantly ($3.35 \pm 1.58$ VS $2.19 \pm 1.45$, $P = 0.001$).

**Conclusion:** EEN is effective for inducing early clinical remission, mucosal healing, promoting fistula closure and reducing the size of abscess to adult CD patients with complications and poor response to drugs. More cases need to be enrolled for further study.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0312 THE EFFICACY OF DOSE SPLITTING THIOPURINES IN HYPERMETHYLATORS

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**Introduction:** Hypermethylation (defined as a methylmercaptopurine to thioguanine nucleotide ratio (MeMP:TGN) of >11) is associated with a poor response to treatment and side effects such as nausea and hepatotoxicity. Conventional management is to switch to low dose thiopurine and allopurinol co-therapy (LDTA). A previous study has shown a significant reduction in MeMP levels through splitting the dose to half in the morning and half in the evening, the rationale being that the reduced dose is below the optimum substrate affinity for the enzyme thiopurine methyltransferase (TPMT).[1].

**Aims & Methods:** We performed a retrospective analysis of patients with inflammatory bowel disease (IBD) who underwent dose splitting. We analysed for: dose, IBD type, ethnicity, TPMT, MeMP:TGN ratio immediately before and after dose splitting, reasons for dose splitting and outcomes as judged by the authors based on whether LDTA was required. Statistical analysis was performed using SPSS. A paired T test was used to make comparisons between the means for TGN, MeMP and MeMP:TGN. TGNs and MeMP are measured in pmol/8 X 108 RBC.

**Results:** 25 patients were identified who underwent dose splitting. 15 were female (Mean age 35.4 years). 13 had Crohn's disease, 1 had IBD unclassified, and 11 had ulcerative colitis. 23 were on azathioprine, 2 were on mercaptopurine. Mean dose was 131 mg for azathioprine and 75 mg for mercaptopurine. 2 patients had dose splitting to 3 daily doses (morning, lunchtime and evening).
Prior to dose splitting, mean MeMP was 4486 (SD 2462), mean TGN was 233 (SD 72) and mean MeMP:TGN was 19 (SD 8.57).
22 patients were dose split due to hypermethylation of which 2 had hepatotoxicity (defined as elevated alanine transferase >45 IU/L). The remaining 3 were dose split for nausea.
9 patients (36%) were no longer hypermethylators after dose splitting. A further 6 patients (24%) had a reduction in the MeMP:TGN ratio but not to >11. 8 patients (32%) were switched to LDTA. 1 patient had no change in the ratio following dose splitting but did have an improvement in their nausea and so continued on dose splitting. 1 patient paradoxically had a higher ratio after dose splitting, but is asymptomatic and has not been switched to LDTA.
Overall, there was a significant reduction in the mean MeMP and the mean MeMP:TGN ratio after dose splitting (4487 versus 3326 ($P < 0.05$) and 19.0 versus 13.2 ($P = 0.01$) respectively). There was no significant change in mean TGN before and after (233 versus 251).
Patients who had hepatotoxicity had no improvement from dose splitting and all were switched to LDTA. There was no significant relationship between gender and TPMT on reduction in MeMP or success with dose splitting.

**Conclusion:** Dose splitting has been shown to significantly reduce both MeMP and MeMP:TGN ratio avoiding the use of LDTA in some patients. Through dose splitting, it is feasible to alter the biochemistry of thiopurine metabolism to reduce hypermethylation whilst maintaining TGNs within a therapeutic range.

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All other authors have declared no conflicts of interest.

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## P0313 NONCLINICAL PHARMACOLOGICAL CHARACTERIZATION AND IN VIVO EFFICACY OF THE PROPOSED ADALIMUMAB BIOSIMILAR GP2017 COMPARED TO THE ORIGINATOR ADALIMUMAB

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**Introduction:** Biosimilars are biologics that are highly similar to already marketed biopharmaceuticals which have lost exclusivity and aim to offer more affordable treatment. Anti-TNF therapeutic antibodies have been shown to be highly effective and safe for the treatment of immune mediated inflammatory diseases such as psoriasis, Crohn's disease and rheumatoid arthritis. Here we present in-vitro functional characterization data of the proposed adalimumab biosimilar GP2017 and in-vivo assessment of reduction in disease progression in homozygous human TNF (huTNF) transgenic murine models of polyarthritis driven by either soluble or membrane bound TNF. The resolution of inflammation upon multiple treatments was compared to the originator adalimumab. Inflammatory markers spanning from clinical signs to histological readouts and related biomarkers were used as endpoints.

**Aims & Methods:** In vitro functional characterization of GP2017 consisted of a cell-based TNFα neutralization potency assay, assays addressing the binding to TNFα, complement component C1q, FcγR and FcRn, as well as assays measuring antibody-dependent cell-mediated cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC) to assess various mechanisms of action ascribed to adalimumab. Untreated, huTNF transgenic mice started to develop severe inflammation at 3–4 weeks of age. Shortly after the onset of disease, two groups of mice were treated twice weekly, either with GP2017 or the originator adalimumab at an intermediate most sensitive sub-therapeutic dose. Two additional groups of mice treated with either placebo or a maximal saturating effective dose of the originator adalimumab served as controls. All animals were sacrificed 3 days after last treatment for histological analysis of joints. Disease scoring system, swelling of the ankles, hind limb distortion, impaired movement as well as progressive weight loss were used as continuous readouts.

**Results:** High degree of similarity was seen in target binding affinity and functional activity for TNFα, Fc-receptors and C1q binding for both GP2017 and originator adalimumab. Correspondingly, bioassays for TNFα neutralization and for Fc dependent effector functions (ADCC and CDC) demonstrated that GP2017 was similar to the originator adalimumab. Comparable in-vivo PD effects were also demonstrated for GP2017 and the originator adalimumab in

murine models of polyarthritis. Significant efficacy in inhibiting the arthritic pathology as well as the underlying histopathology, was seen with both GP2017 and the originator adalimumab, as compared to placebo treated animals.
**Conclusion:** GP2017 and the originator adalimumab exhibited similar in vitro pharmacology and in vivo efficacy in TNF driven disease models of polyarthritis. In combination with structural and physicochemical characterization and pre-clinical pharmacokinetics and safety, similarity of GP2017 and the originator adalimumab was demonstrated at the nonclinical level. Ongoing clinical trial (s) aim to provide additional confirmatory evidence of similar efficacy and safety of GP2017 compared to the originator adalimumab, further minimizing the remaining residual uncertainty.
**Disclosure of Interest:** A. da Silva: I am an employee of Sandoz Biopharmaceuticals.
C. Fritsch: I am an employee of Novartis Pharma AG.
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## P0314 VEDOLIZUMAB: EARLY EXPERIENCE AND MEDIUM-TERM FOLLOW-UP DATA FROM TWO UK TERTIARY IBD CENTRES – A RETROSPECTIVE COHORT STUDY

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**Introduction:** Vedolizumab, a selective leukocyte adhesion molecule inhibitor, has recently been granted approval for use in moderate-to-severe Crohn's disease (CD) and ulcerative colitis (UC). Novel inflammatory bowel disease (IBD) pathways agreed by our local clinical commissioning group meant that patients at Guy's & St. Thomas' (GSTT) and King's College Hospitals (KCH) had access to vedolizumab from November 2014, prior to NICE approval, which was not granted until June 2015.
**Aims & Methods:** The records of patients with IBD commencing vedolizumab at GSTT and KCH between November 2014 and November 2015 were screened and those completing at least 14 weeks of treatment were included. Outcome assessments were made by retrospective review of prospectively maintained records. Clinical disease activity was assessed using Harvey-Bradshaw Index (HBI) or Simple Clinical Colitis Activity Index (SCCAI) at baseline, 14 and 30 weeks of treatment. Response was defined as HBI/SCCAI reduction $\geq$3. Remission was defined as HBI $<$ 5 or SCCAI $<$ 3. Primary outcome:.
- Change in clinical disease activity Secondary outcomes:.
- Change in biochemical markers of disease activity (CRP and faecal calprotectin).
- Rates of corticosteroid usage and surgery Sixty-two patients received at least one infusion of vedolizumab for CD, UC or IBD-unclassified (IBD-U). Patients who had not completed at least 14 weeks of treatment (n = 5), had missing clinical disease activity data (n = 2) or a stoma (n = 5) were excluded from further analysis. Continuous data are summarised as medians followed by range. Pre- and post-induction values were compared using Wilcoxon signed-rank test.
**Results:** Primary Outcome: Of the 50 patients whose data were analysed, 27 had CD, 20 had UC and 3 had IBD-U (included in the UC group for the purpose of analysis). At baseline visit the median HBI was 8 (1–16) and SCCAI was 6 (0–15). At week 14 these values had fallen to 5 (0–15) (p = 0.117) and 4 (0–10) (p = 0.005), respectively. Additional week 30 data was available for 19 patients (9 CD, 10 UC). The clinical disease activity scores at that point were HBI 2 (0–7) and SCCAI 2 (1–10), reflecting a significant fall from baseline values and remission in both cases (p = 0.039 and p = 0.023, respectively) At baseline, 37 (74%) of the 50 patients had clinically active disease (HBI $\geq$ 5, SCCAI $\geq$ 3). Of the patients with active disease, 22 (59%) responded and 14 (38%) achieved remission. Divided by IBD-subtype, response rates were 12/19 (63%) in CD and 10/18 (55%) in UC. Remission rates were 7/19 (37%) in CD and 7/18 (39%) in UC. Divided by prior anti-TNF exposure, response rates were 5/8 (63%) in anti-TNF naïve and 17/29 (59%) in anti-TNF exposed patients. Corresponding remission rates were 5/8 (63%) and 9/29 (33%), respectively. Of the 13 patients with inactive clinical disease at baseline, 8 (62%) remained in remission at week 14.
Secondary Outcomes: Faecal calprotectin fell significantly, pre-treatment: 1076 (27-4800), post-week 14: 476 (10-3184) (p = 0.010 for n = 18). CRP remained stable, baseline: 4 (1–70), week 14: 4 (1–72) (p = 0.627 for n = 49). Rates of steroid use at each study time point were 24/50 (48%) at baseline, 16/50 (32%) at week 14 and 3/19 (16%) at week 30 (p = 0.008). Surgery was required in 4/50 (8%, 3 CD 1 UC).
**Conclusion:** Our experience mirrors a previously reported 'real-world' cohort[1] and demonstrates similar efficacy to those reported in the GEMINI trial program[2, 3]. This data demonstrates a meaningful reduction in clinical and biochemical disease activity as well as a steroid-sparing effect in patients with complex and previously refractory disease. Outcomes were more favourable amongst anti-TNF naïve patients than those with previous exposure but did not significantly differ between UC and CD.
**Disclosure of Interest:** M. Samaan: Advisory board: Hospira Lecturing and training: Hospira, Takeda, MSD.
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All other authors have declared no conflicts of interest.

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## P0315 HIGHER EXPOSURE BUT LOWER RESPONSE RATE TO INFLIXIMAB INDUCTION THERAPY IN ELDERLY PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Infliximab (IFX) is used less frequently in elderly patients ($\geq$65 years) with moderate-to-severe Crohn's disease (CD) and ulcerative colitis (UC) due to lower efficacy and higher risk of adverse events compared to younger patients (1). The ageing process has been associated with physiological and immunological changes that might influence the pharmacokinetics (PK) of IFX and thereby its efficacy. However, no data are available on the IFX exposure-response relation in elderly patients with inflammatory bowel disease (IBD).

**Table 1:** Infliximab trough concentrations, mean ± standard deviation (number of patients), and patient baseline characteristics in non-elderly and elderly patients with inflammatory bowel disease.

| | Non-elderly | Elderly |
|---|---|---|
| **Trough concentrations (μg/mL)** | | |
| **Week 2** | 25.7 ± 16.0 (n = 51) | 25.6 ± 12.4 (n = 30) |
| **Week 6** | 16.8 ± 11.7 (n = 48) | 19.3 ± 14.3 (n = 26) |
| **Week 14 *** | 5.7 ± 4.8 (n = 42) | 9.5 ± 5.9 (n = 14) |
| **Baseline characteristics** | | |
| **Female, n (%)** | 24 (44) | 19 (63) |
| **Age, median [IQR], years **** | 37 [27–50] | 69 [66–74] |
| **Charlson Comorbidity Index > 0, n (%) *** | 13 (24) | 14 (47) |
| **Disease duration, median [IQR], months** | 59 [21–428] | 101 [32–270] |
| **UC/CD/IBDU, n (%) *** | 16/12/2 (80/20/0) | 43/11/0 (53/40/7) |
| **Albumin < 35 g/L, n (%) **** | 3 (9) | 11 (38) |
| **CRP > 5 mg/L, n (%)** | 29 (54) | 21 (72) |
| **Lean body mass, median [IQR], kg ***** | 52 [46–61] | 46 [40–52] |

* p < .05, ** p < .01, *** p < .001, **** p < .0001. Lean body mass calculated using James formula. Multivariate linear regression withheld age $\geq$65 years as an independent predictor of higher TC at w6 and w14, but not at w2. A serum albumin concentration (SAC) < 35 g/L at w2, w6 and w14 was identified as an independent predictor of a lower TC at the respective time point. The proportion of patients with SAC < 35 g/L at w2 was significantly higher in elderly patients (27%, 7/26) compared to non-elderly patients (4%, 2/50) (p = .006), while at w6 and w14 proportions were similar in both groups. SAC $\geq$ 35 g/L at w2 is associated with clinical response (p = .003) and biological response (p = .02). Elderly patients had a significantly lower lean body mass at w6 (46 ± 1 kg) and w14 (48 ± 2 kg) compared to the non-elderly controls (54 ± 1 kg and 56 ± 1 kg, resp.) (p = .0004 and p = .005, resp.), but when adjusted for the lean body mass, the effect of age on the TC was still significant. Using a drug tolerant assay, 7% of the elderly (1/14) and 17% of the non-elderly (7/41) patients were identified as ATI+ at w14. The proportion of short-term clinical and biological responders to IFX induction therapy was lower among elderly patients (67% and 38%, resp.) compared to non-elderly patients (85% and 71%, resp.) (p = .047 and p = .040, resp.).

**Aims & Methods:** The aim of this retrospective, tertiary single-center case-control study was to analyze the exposure-response relation to IFX during induction therapy in 30 consecutive elderly cases (16 UC, 12 CD, 2 IBD unclassified) and 54 non-elderly controls (43 UC, 11 CD) (controls matched 2:1 to cases for follow-up and disease duration). IFX trough concentrations (TC) were measured

in consecutive trough samples and antibodies towards IFX (ATI) were measured in w14 samples using in-house developed ELISAs. IFX TC and their relation to short-term clinical (based on physician global assessment) and biological response (defined as a CRP $\leq$ 5 mg/L by w14) were evaluated. Patient- and disease-related factors were analyzed in multiple linear regression (backward selection, $\alpha = 5\%$) with TC as dependent variable.
**Results:** Elderly patients did not have significantly different IFX TC at w2 and w6 compared to the respective non-elderly controls (table 1). TC at w14 were significantly higher in elderly patients compared to the non-elderly controls ($p = .02$).
**Conclusion:** Elderly age is independently associated with higher IFX TC, nonetheless, rates of short-term clinical and biological response were lower in the elderly patients.
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A. Gils: A. Gils Lecture fee (s): MSD, Janssen Biologicals, Abbvie, Pfizer, Takeda. Consultancy: UCB. Conflict with: license of infliximab, anti-infliximab and adalimumab ELISA from Institution to apDia and with lateral flow infliximab to R-Biopharm AG.
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All other authors have declared no conflicts of interest.

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### P0316 ANTI-TNFA ANTIBODY INDUCED PSORIASIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE; A PROSPECTIVE IRISH COHORT STUDY

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**Introduction:** The increased use of anti-TNF$\alpha$ antibody in Inflammatory Bowel Disease (IBD) has generated interest regarding adverse events of this relatively new therapeutic option, including the paradoxical triggering of psoriatic skin lesions.
**Aims & Methods:** To determine the prevalence of psoriasis in an IBD cohort with reference to clinical characteristics and anti-TNF$\alpha$ use. Following ethical approval, a survey questionnaire that included demographic and clinical data including age, gender, smoking status, IBD type, diagnosis of psoriasis and anti-TNF$\alpha$ use was devised and posted out to all patients attending the IBD clinic in Tallaght Hospital. Incidence rates of concomitant and reactive psoriasis were calculated and compared using a students T-test. A p value of $<0.05$ was considered significant.
**Results:** In all, 905 questionnaires were posted out, 34% (n = 312) returned, 32% (n = 286) were complete. In all, 58% (n = 166) were female, 36% (n = 103) and 64% (n = 183) had UC and CD respectively, 55% (n = 157) ever smoked, 44% (n = 126) were ever on an anti-TNF$\alpha$ therapy of which 56% (n = 71) had been on Adalimumab (ADA) only, 18% (n = 23) Infliximab (IFX) only, 23% (n = 29) on ADA or IFX, and 2% (n = 3) were exposed to Symponi. In all, 55.3% (n = 57) and 54.6% (n = 100) of the UC and CD cohort smoked. The overall prevalence rate of IBD and psoriasis was 9.4% (n = 27), mean age 48 years (range 33–66) of which 30% (n = 8) had reactive psoriasis, ie psoriasis occurring after commencement anti-TNF$\alpha$ therapy. The mean duration of treatment before onset of reactive psoriasis was 2.6years. The prevalence rate of psoriasis in the non-biologic and biologic cohort was 11.9% (19 of 160) and 6.3% (8 of 126) respectively, p = 0.1, CI = 1.82 to 12.57. There was a similar rate of the overall prevalence of IBD and psoriasis 9.4% (27 of 286) compared to reactive psoriasis 6.3% (8 of 126), p = 0.31, CI = 3.52 to 8.40 in our cohort. Interestingly, all 8 patients who had reactive psoriasis had CD and were female compared to 63% (17 of 27) CD and females in the overall psoriasis group, p = 0.04, CI = 3.93 to 57.59. There was no association between the type of AntiTNF$\alpha$ prescribed with the occurrence of reactive psoriasis 6% (6 of 100) vs. 3.8% (2 of 52) ADA and IFX respectively, Odds Ratio (OR) = 1.5, p = 0.59, 95% CI 0.30 to 8.00 or smoking with any form of psoriasis in IBD, OR = 1.4, p = 0.42, CI = 0.6182 to 3.1560.
**Conclusion:** In our study, there was a similar prevalence rate of reactive psoriasis and background rate of psoriasis in the overall IBD cohort (6.3% vs 9.4%). Our study suggests that the risk factors associated with reactive psoriasis include a diagnosis of CD and female gender. Further work to elucidate the pathophysiology of this phenomenon is required.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0317 A RANDOMIZED CONTROLLED TRIAL ON YOGA FOR ULCERATIVE COLITIS

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**Introduction:** Ulcerative colitis is associated with marked impairments in all aspects of quality of life. Yoga is a mind-body practice which is used for health purposes. Various styles of yoga typically combine physical postures, breathing techniques, and meditation or relaxation.
**Aims & Methods:** Patients with ulcerative colitis in clinically remission (CAI) and impaired quality of life (Inflammatory Bowel Disease Questionnaire [IBDQ] < 170) were randomly assigned to hatha yoga (one weekly session of 90 minutes over 12 weeks) or written lifestyle advice. The primary outcome measure was disease-specific Quality of life (IBDQ). Secondary outcomes included generic quality of life (SF-36), disease ctivity (Clinical Activity Index), anxiety and depression (Hospital Anxiety and Depression Scale), positive and negative affect (Positive and Negative Affect Schedule), perceived stress (Perceived Stress Scale, Perceived Stress Questionnaire), and self-efficacy (General Self-Efficacy Scale), laboratory parameters and fecal inflammation markers (calprotectin, lactoferrin, PMN-elastase). Outcomes were assessed at week 12 and week 24 after randomization by blinded outcome assessors.
**Results:** A total of 77 patients (75% women; 45.5 ± 11.9 years; 13.4 ± 8.8 years since diagnosis; CAI = 2.2 ± 1.5; IBDQ = 144.9 ± 23.4) were randomized to yoga (YG; n = 39) or control (CG; n = 38). After 12 weeks, the yoga group had significantly higher disease-specific quality of life compared to the control group (IBDQ: YG = 158.8 ± 32.2; CG = 147.1 ± 36.0; p = 0.018). Significant group differences were also found for physical quality of life (p = 0.030), anxiety (p = 0.019), depression (p = 0.001), and self-efficacy. All effects were maintained at week 24 (IBDQ: YG = 167.8 ± 29.2; CG = 153.1 ± 35.9; p = 0.022); additionally, significant group differences at week 24 were found for disease activity (p = 0.029), mental quality of life (p = 0.009), positive affect (p = 0.020), perceived stress (p = 0.020), and self-efficacy (p = 0.019).
**Conclusion:** A 12-week yoga intervention improved quality of life and mental health in patients with ulcerative colitis. The effects persisted for at least 3 months after the end of the intervention. Yoga can thus be regarded as a complementary intervention for patients with ulcerative colitis.
**Disclosure of Interest:** J. Langhorst: Research grant: TechLab, Steigerwald, Falk Foundation lecture honorarium: Falk; MSD; Repha; Ardeypharm.
All other authors have declared no conflicts of interest.

### P0318 A LOW FODMAPS DIET REDUCES FUNCTIONAL SYMPTOMS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE WITH NO SIGNS OF ACTIVE INFLAMMATION

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**Introduction:** FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols) indicate a series of osmotically active and rapidly fermentable compounds that may lead to functional gastrointestinal symptoms (bloating, abdominal pain, wind, diarrhoea). Patients with Inflammatory Bowel Diseases (IBD) can experience functional gastrointestinal symptoms not related to inflammation, but in literature data about the use of low FODMAPs diet in this setting are scarce.
**Aims & Methods:** The aim of our study was to evaluate the usefulness low FODMAPs diet in patients with non active IBD compared to patients with irritable bowel syndrome (IBS). From March 2015 to September 2015 we performed a dietetic interventional prospective study evaluating the effect of a low FODMAPs diet in patients with IBS and IBD with no signs of active inflammation but experiencing apparent functional symptoms (e.g. bloating, diarrhoea, flatulence). The definition of state of remission for IBD subjects was made in accordance with the ECCO guidelines (clinical remission in CD: CDAI < 150; clinical remission in patients in UC: Mayo score < 2). The diagnosis of IBS has made by using the Rome III criteria. Each subject was submitted to a diet low in FODMAPs, after filling out questionnaires on quality of life and symptoms (SF-36 and IBS-SSS). After the administration of the questionnaires, an experienced dietician explained the diet low in FODMAPs to patients. Each regimen was specific for the patient's energy requirement (calculated by BMI) and for its content in FODMAPs, realized in conformity with the food reference tables. The low FODMAPs diet was prescribed for 2–6 weeks, after which a steady re-introduction phase was followed, and closely monitored, until a balance between tolerated doses and symptom control was achieved.
**Results:** The study included 65 patients (22 with IBD and 43 with IBS). The analysis of the IBS-SSS survey showed that functional symptoms improved after 1 month and after 3 months of low FODMAPs diet, both in patients

with IBD and in those with IBS, with no statistically significant difference between the two groups (overall score IBD: 2.01 at T0, 1.23 at T1 and 1.00 at T3 ($p < 0.01$); overall score IBS: 2.37 at T0, 1.43 at T1 and 1.08 at T3 ($p < 0.01$). Furthermore, also by using the SF-36 questionnaire, we did not observe any statistically significant difference between the two groups in terms of response to diet ($p = NS$), even if a trend of clinical improvement was described at 1 month and 3 months after the start of the diet, for all 8 domains of the questionnaire. On the other hand, a statistically significant difference between the two groups was evident before starting the dietary approach. In particular, for some domains (role physical, bodily pain, social functioning, role emotional state), patients with IBD had a significantly greater perception of symptoms compared to patients with IBS. This would reinforce the concept that, in patients with CD or UC in remission, residual symptoms are attributable to the presence of functional disorders, comparable to those of IBS. These symptoms could improve by using a low FODMAPs diet.

**Conclusion:** A low FODMPs diet can improve functional symptoms in patients with IBS and in subjects with IBD that experience symptoms not due to active disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0319 FAECAL MICROBIOTA TRANSPLANTATION (FMT) AS A RESCUE THERAPY FOR STEROID-DEPENDENT AND/OR NON-RESPONSIVE PATIENTS WITH ULCERATIVE COLITIS (UC): A PILOT STUDY

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**Introduction:** FMT is an experimental method for restoration of dysbiosis in UC. Few studies reported improvement in clinical and endoscopical response. However, route of administration, donor and patient selection, number of FMT sessions and intervals are still obscure. Steroid failure leads the patient to a next step of drugs. Immunomodulatory or biological agents have higher costs and adverse events, potential risks of infection and malignancy. We have analysed the efficacy of rescue FMT for steroid-dependent and/or non-responsive UC patients.

**Aims & Methods:** Fourteen patients with steroid-dependent and/or non-responsive UC were enrolled, and treated with FMT. Follow-up clinical data was collected for at least 3 months (3–18 months). Donors were selected according to Amsterdam Criteria. All patients received FMT after complete colon cleansing via colon. Patient and donor clinical, demographic and laboratory data were recorded.

**Results:** Eleven of fourteen (78.5%) patients achieved clinical improvement and were able to discontinue steroids following rescue FMT. One patient was lost to follow-up. Among the 11 patients who responded, five (45.4%) received one FMT therapy, one (9.0%) received two FMTs, and three (27.2%) received four FMTs, and two (18.1%) received six FMTs. Six (54.5%) of the 11 patients who responded maintained long-term remission during follow-up (3–18 months). Three patients (21.4%) failed to meet the criteria of clinical improvement and maintained steroid dependence, though one patient experienced transient or partial improvement. Eight of 11 responders had the same blood group antigen with the corresponding donor. Patient age ($28 \pm 8$ vs $47 \pm 11$yrs, $p < 0.05$) and disease duration ($6 \pm 3$ vs $35 \pm 12$ months, $p < 0.05$) were also lower in responders. Mean body mass index ($kg/m^2$) increased in all responders (baseline: $23 \pm 3$ vs post-FMT 3 months: $26 \pm 2$, $p < 0.05$). None of the patients experienced major adverse events due to FMT.

**Conclusion:** Rescue FMT shows promise as a therapeutic strategy for patients with steroid-dependent and/or non-responsive UC, likely due to the successful restructuring of gut microbial composition. Blood group antigen-match might be a promising research area such as in other organ transplantations. Post-FMT weight gain might be due to cessation of inflammation or improved dysbiosis. Further studies are urgently needed to clarify predictive factors of success for FMT in this population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0320 INDIGO NATURALIS ALTERS THE GUT MICROBIAL COMMUNITY AND MODIFIES COURSE OF INFLAMMATION IN THE MOUSE MODEL OF COLITIS

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**Introduction:** Indigo Naturalis (IND), also known as 'Qing Dai', is a herbal medicine which has been traditionally used for the treatment of inflammatory lesions including skin rush, psoriasis and ulcerative colitis in China. Especially, the effect on Ulcerative colitis (UC) has been attracting some attention due to some recently reported clinical studies showing good effect of IND on active UC. One showed that clinical response and mucosal healing reached to 72% and 61%, respectively in moderate UC patients, and another showed it helped six of seven patients to reduce and discontinue corticosteroid, which sounds promising. However, the mechanism of action or possible adverse events has not been well studied in the basic research. The aim of study was to investigate the effect of IND for the treatment of colitis and how it works.

**Aims & Methods:** A mouse model of Th2-type colitis, oxazolone (OXA) colitis, was used. OXA colitis was induced in BALB/c mice by rectal injection of 0.5% OXA one week after sensitization of OXA by skin painting. After induction of colitis, mice were fed with 5% IND-mixed chow. The severity of colitis was evaluated by body weight change, colonoscopy scoring, histology of the colonic tissues, and the gene expression levels of inflammatory cytokines in the colon were also tested by real-time PCR. To analyze whether IND can influence the composition of the gut microbiota, fecal samples from IND fed and non-fed colitic mice were collected and they were subjected to the 16 S ribosomal RNA gene sequencing.

**Results:** IND treatment significantly reduced the expression of IL-13, the cytokine shown to induce inflammation in the OXA colitis model, however, the severity of colitis was aggravated along with the upregulation of TNF$\alpha$ in the IND fed mice. We also found that the result of 16 S ribosomal RNA sequencing showed a dramatic change of the composition of gut microbiota in the IND fed mice compared to IND non-fed mice. To test whether this change conferred to the aggravation of colitis, we treated the mice with 4 antibiotics (ampicillin, vancomycin, metronidazole, and neomycin) to deplete the gut microbiota, and then OXA colitis was induced. As we expected, the aggravation of colitis was reversed and the level of colitis became similar between IND fed mice and non-fed control mice.

**Conclusion:** Needless to say, the results of experiments using animal disease model should be carefully interpreted, and obviously, should not be directly applied to human case. Furthermore, the amount of IND given to mice in our study could be too large/small than those optimal doses used for UC treatment. Therefore, further experiments with different doses of IND should be tested. However, the result of our study clearly showed that IND has an ability to change the composition of gut microbiota. With recent reports of fecal microbiota transplant expected to be a new strategy to treat UC patients in the future, it is now widely recognized that gut microbiota plays an important role in the pathogenesis of UC. Our result suggests that IND has a potential to be used for the treatment of UC, or to cause unwanted adverse events through modifying gut microbiota. Further basic research on IND would be required, and clinical trials should be carefully conducted.

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## P0321 TRENDS IN ENDOSCOPY MANAGEMENT AFTER SURGERY IN A NATIONAL COHORT OF SPANISH CROHN DISEASE PATIENTS: RESULTS FROM PRACTICROHN STUDY

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**Introduction:** Recurrence of Crohn disease (CD) after an ileo-colonic resection is predicted by the severity of endoscopic lesions during the first year after resection, hence guidelines recommend every patient to underwent endoscopy during the first year after surgery. The aim of our study was to describe the management and results of endoscopy after surgery in a population of CD patients between 2007 and 2010.

**Aims & Methods:** PRACTICROHN was a retrospective study that included patients aged ≥18 years-old from 26 Spanish hospitals who underwent CD-related ileocolonic or ileorectal resection with ileocolonicor ileorectal anastomosis between January 2007 and December 2010. Clinical data was retrospectively collected from clinical charts.Categorical variables were compared with the $\chi 2$ test or Fisher'sexact test, Kaplan-Meier method was used to assess time to clinical recurrence and a log-rank test to obtain statistical significance.

**Results:** 314 patients were analyzed (mean age 40 years [SD 13], 48% men). Of these, 52 (16.56%) had suffered previous surgeries. In 143 (46.28%) a colonoscopy was performed during the first year after surgery. In 2007, only 24/75 patients (33%) underwent endoscopy in the first year, while in 2010 endoscopy was performed in 47/79 (59.49%) $p = 0.017$. During first year after surgery, 146 (46.50%) patients presented with endoscopic recurrence without symptoms.

Along the five years follow-up 222 patients underwent colonoscopy. Rutgeerts score was ≥ 2 in 122 patients (54.9%). Rutgeerts score in patients that received prophylactic treatment was significantly lower than in patients without prophylaxis.

**Table**

| | | Prophylactic treatment Yes | No | p |
|---|---|---|---|---|
| Rutgeerts score | 0 | 54 (37.24) | 15 (20.83) | 0.005 |
| | 1i | 18 (12.41) | 11 (15.28) | 0.005 |
| | 2i | 40 (27.59) | 16 (22.22) | 0.005 |
| | 3i | 12 (8.28) | 18 (25.00) | 0.005 |
| | 4i | 21 (14.48) | 12 (16.67) | 0.005 |

**Conclusion:** In the time interval of data collection of the study there was a trend towards performing significantly more endoscopies after surgery in CD patients, as recommended by guidelines. The number of endoscopic recurrence without symptoms in our study reinforces the importance of performing colonoscopies in high risk CD patients. Prophylactic treatment after surgery is associated with lower Rutgeerts score and prevents endoscopic recurrence.
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C. Romero: Full time employee for MSD Spain.
B. Juliá De Páramo: Full time employee for MSD Spain.
All other authors have declared no conflicts of interest.

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### P0322 USE OF ANTI-TNF AGENTS IS ASSOCIATED WITH PARADOXICAL PSORIASIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A KOREAN NATIONWIDE POPULATION-BASED STUDY


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**Introduction:** It has been reported that use of anti-tumor necrosis factor (anti-TNF) agents may be associated with paradoxical dermatologic complications such as psoriasis.
**Aims & Methods:** A cross-sectional nationwide population study was performed by using the Korea National Health Insurance Claim Data. A total of 42, 165 inflammatory bowel disease (IBD) patients consisting of ulcerative colitis (UC) (n = 29, 434) and Crohn's disease (CD) (n = 12, 731) were identified between 2009 and 2013. Among them, those who were treated with any anti-TNFs more than 6 months were 1, 664 (3.9%). Thirty-three IBD patients who had co-existing psoriasis in 2009 were excluded. One-to-five age- and sex-matched controls were randomly sampled to compare incidences of psoriasis, psoriatic arthritis, and palmoplantar pustulosis (PPP) between the patients with and without anti-TNF treatment.
**Results:** Incidence of psoriasis was significantly higher in IBD with anti-TNF group (31/1, 631; 1.90%) compared with IBD without anti-TNF group (64/8, 057; 0.79%) (adjusted odds ratio [aOR] 2.44; 95% confidence interval [CI] 1.58 to 3.76; $p < 0.0001$). Psoriatic arthritis and PPP also showed higher incidence in IBD with anti-TNF group (aOR 1.71; 95% CI 0.86–3.40 and aOR 3.77; 95% CI 1.31–10.90, respectively). In subgroup analyses, aORs for psoriasis by IBD subtype were 2.03 (95% CI 0.78–5.27) in UC and 2.57 (95% CI 1.58–4.18) in CD. aORs for psoriasis by gender were 2.21 (95% CI 1.25 to 3.93) in male and 2.79 (95% CI 1.44 to 5.42) in female. aORs for psoriasis according to age groups were 2.97 (95% CI 1.07 to 8.24) under 20 years old, 2.68 (95% CI 1.57 to 4.56) between 21 to 39, and 1.47 (95% CI 0.48 to 4.51) aged 40 and over, which implies younger IBD patients have a higher risk of anti-TNF-induced psoriasis.
**Conclusion:** The risk of psoriasis is increased by anti-TNF agents in patients with IBD and higher especially in younger patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0323 COMBINATION THERAPY PREDICTS LONG-TERM MUCOSAL HEALING IN MODERATE-TO-SEVERE ULCERATIVE COLITIS TREATED WITH ANTI TNF-A


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**Introduction:** Mucosal healing (MH) has emerged as an important treatment goal in ulcerative colitis, because can alter the course of the disease. The aim of our study was to evaluate long-term MH of a large cohort of moderately-to severely active ulcerative colitis (UC) patients treated with anti Tumor necrosis factor (TNF)-α and to explore predictors of efficacy thereof.
**Aims & Methods:** We retrospectively collected data on all consecutive outpatients with moderate-to severe UC who started anti TNF-α at our IBD center from January 2008 to June 2015. Associations between clinical and epidemiological characteristics and clinical remission and MH were analyzed with survival regression models and expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). Clinical remission was defined as disappearance of diarrhoea and blood, without corticosteroids for at least 6 months. MH was defined as a Mayo endoscopy subscore of 0 or 1.[a].
**Results:** A total of 160 patients started anti TNF-α during the interval. The mean (SD) age at diagnosis was 39 (14) years and the median duration of disease was 4 years (range 2–9 years). One-hundred and four patients (65%) had pancolitis and 56 (35%) left-sided colitis. Thirty-nine patients (24%) were started on concomitant thiopurines. After a median of 9 months, 108 (68%) patients achieved clinical remission. Duration of disease (HR 0.95, 95% CI 0.90, 1.00) and anti TNF-α dose optimization (HR 0.49, 95% CI 0.26, 0.92) were inversely associated with worse clinical outcome. MH was recorded in 71 patients (55%), after a median time to endoscopy of 27 months (range 22–32). Anti TNF-α combination therapy (HR for monotherapy vs combination therapy 0.16, 95% CI 0.21, 0.87) and clinical remission (HR 0.14, 95% CI 0.07, 0.23) were inversely associated with persistent endoscopic activity.
**Conclusion:** Long-term anti TNF-α treatment is effective in inducing MH in patients with moderate-to-severe UC. Combination therapy led to significantly better MH than anti TNF-α monotherapy.
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All other authors have declared no conflicts of interest.

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### P0324 ADSORPTIVE DEPLETION OF MYELOID LINEAGE LEUCOCYTES IN PATIENTS WITH ULCERATIVE COLITIS: BASELINE DEMOGRAPHIC FEATURES OF NON-RESPONDERS AND RESPONDERS TO THIS APHERESIS TREATMENT OPTION


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**Introduction:** Patients with active inflammatory bowel disease (IBD) have elevated myeloid lineage leucocytes like the CD14 (+) CD16 (+) monocyte phenotype, which is a major source of tumour necrosis factor-α (Belge, et al. *J Immunol* 2002). Hence depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn is expected to promote remission or at least enhance drug efficacy. However, studies in ulcerative colitis (UC) have reported contrasting efficacy, from an 85% (Suzuki, et al. *Gastroenterology* 2005) to a statistically insignificant level (Sands, et al. *Gastroenterology* 2008). Patients' demographic variables in the aforementioned studies were different.

**Aims & Methods:** In 145 UC patients who had undergone GMA therapy at our institute over the past 10 years, we looked at baseline clinical and endoscopic features of responders and non-responders to GMA. Seventy-three 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) $\leq 4$ was defined as response to GMA. Biopsies from colonoscopically detectable inflamed mucosa were processed to see the impact of GMA on leucocytes within the mucosa.
**Results:** At baseline, the average CAI was 12.8, range 10–17. Ninety-three 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. Upon relapse, the majority of patients responded well to a second course of GMA. Over 1200 biopsies were processed. Infiltrating leucocytes were mostly neutrophils and monocytes. There was a marked reduction of infiltrating leucocytes in responders. Patients with extensive deep UC lesions together with loss of the mucosal tissue at the lesions were identified as non-responders. Patients with the first UC episode were identified as the best responders (100%), followed by steroid naive patients. Additionally, a short duration of active UC prior to GMA marked a patient as a likely responder.
**Conclusion:** Depleting elevated myeloid lineage leucocytes was associated with efficacy in UC patients, most notably first episode and steroid naïve cases who attained a favourable future clinical course. Additionally, GMA was more effective if applied immediately after a relapse than after a lag time. In general, GMA is very much favoured by patients for its safety profile and for being a non-drug therapeutic intervention. 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 stop futile use of medical resources.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0325 EFFICACY OF TUBERCULOSIS SCREENING IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Inflammatory bowel disease (IBD), by their own impact on the immunity of our patients, malnutrition and increased use of immunosuppressive treatments determine a group at risk of developing active tuberculosis (AT).
**Aims & Methods:** The aim of this study was to report the outcome of the screening of latent tuberculosis and the effectiveness of the latter in the prevention of AT. We collected retrospectively patients' records between January 2010 and December 2014 who underwent a tuberculosis screening including at least one Tuberculin Skin Test (TST), chest radiography (CR) (a CT scan was done when doubt on the CR) with or without a blood test: QuantiFERON®–TB Gold In-Tube test (QTF). This has occurred as part of a pre- therapeutic assessment or systematically. We also studied the appearance of a possible subsequent AT.
**Results:** We have studied 123 cases. They were 70 men and 53 women. Smokers or weaned smokers were a total of 36. The average age was 33.24 years and average BMI 20.9 kg/m$^2$. Diabetics or hypertensives numbered 4 each. 7 patients had an ulcerative colitis (UC) which was a pancolitis in all cases. 116 patients had Crohn's disease (CD). In the 6 months before screening tests: 25% of patients were under salicylates, 40.8% under corticosteroids, 44.16% azathioprine (AZA) and 10% under anti-TNF alpha. Patients were in flair-up at screening test in 67.5% of cases, it was a severe one in 36.6% of cases. Biology at the time of the tests: average CRP 71.82 mg / L, an average of 28.8 g/l albumin and hemoglobin average of 10.35 mg / dl. All patients had a TST and a CR, 99 of them (80.4%) had a QTF. 9 had a positive TST, 3 a positive CR and 7 a positive QTF. 4 patients had indeterminate QTF, they were all in severe flares of their disease, and were all under azathioprine, two under AZA and steroids. Chemoprophylaxis was prescribed in all 4 cases. No cases of AT were noted. As for the anti- tubercular chemoprophylaxis, 27 patients (22%) have benefited of it: 13 for a positive test (latent TB), 7 for an immunosuppression (drug-induced) and 7 for malnutrition (low BMI –biological findings).

AT cases under immunosuppressive therapy

| | |
|---|---|
| Number | 5 (4.1%) |
| Received treatment before AT | 3: ATF / 2: ATF + AZA |
| Average time to AT | 7 months |
| localization | 3 pulmonary-1 ganglionic-1 péritoneal |
| Positive screening | All negative including QTF. |
| Chemoprophylaxis | prescribed in 3 cases for malnutrition |

**Conclusion:** Despite pretreatment comprehensive assessment including TST, CR and QTF. And despite a relative wide prescription of anti- tubercular chemoprophylaxis, 4.1% of our patients developed active tuberculosis undergoing immunosuppressant treatment. This pre- therapeutic assessment is certainly necessary, especially in an endemic country like ours, but is still of limited effectiveness since all our patients who developed tuberculosis reactivation had a negative screening.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0326 EXCLUSIVE ENTERAL NUTRITION IN ADULTS WITH ACTIVE CROHN'S DISEASE IS ASSOCIATED WITH DEACRSE IN DISEASE ACTIVETY

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**Introduction:** Exclusive Enteral Nutrition (EEN) for 8–12 weeks induces clinical remission in $\sim 70\%$ in children and adolescents with active Crohn's disease (CD), and is considered comparable to steroids. Nonetheless, in adults EEN has not gained acceptance. We aimed to evaluate the impact of EEN in adult patients with active CD.
**Aims & Methods:** Patients with active CD referred for nutritional intervention with EEN in a tertiary inflammatory bowel disease (IBD) center were enrolled. All patients were assessed by the centers' gastroenterologists and nutritionist. Baseline metabolic status, weight and nutritional needs were evaluated. EEN was administered either as a polymeric or a hydrolyzed formula. Patients were treated for at least three weeks and were tightly followed by the nutritionist. Physician's Global assessment (PGA), Harvey Bradshaw Index (HBI), biomarkers (blood count, C-reactive protein [CRP], albumin), weight, and body mass index (BMI) were measured and recorded at baseline and at the end of EEN treatment.
**Results:** A total of 25 patients with active CD started EEN. Demographics: The mean age was $31.7 \pm 9.4$ years; Male/female ratio 9/16. Average BMI $21.8 \pm 4.1$ kg/m$^2$; median disease duration 9.5 (IQR 1-22) years. Ten patients (40%) had newly diagnosed CD (range 3–18 months). Location: L1 (ileal)- 10/25 (40%), L3 (ileocolonic)-13/25 (52%); Behaviour: B2 (stricturing) -9/25 (36%), B3 (penetrating)- 5/25 (20%); P (perianaldisease)- 7/25 (28%). Baseline disease activity: PGA – mild-5, –moderate-13, and severe-7; mean HBI $6.95 \pm 5.3$ points; median CRP 1.75 mg/dl (IQR 1.0–3.8), and mean albumin $3.86 \pm 0.5$ mg/l. Twelve patients (48%) were on stable doses of biologics, thiopurines, corticosteroids or mesalamine, and four (16%) were treated with EEN only. Mean EEN duration was 5.75 weeks (range 3–16). PGA improved in 19/20 patients. Baseline vs. end of EEN outcomes: HBI $6.75 \pm 5.5$ vs. $2.75 \pm 3.4$ points ($p = 0.001$); median CRP 1.75 (IQR 1.0–3.8) vs. 0.53 (IQR 0.4–0.93) mg/dl ($p = 0.001$);mean albumin $3.9 \pm 0.52$ vs. $4.3 \pm 1.2$ mg/l ($p = 0.001$). No significant change in weight and BMI was observed. The improvement in most activity measures was noticed in patients with newly diagnosed, as well as long standing disease: HBI drop-$5.1 \pm 4.2$ to $1.5 \pm 1.4$ points ($p = 0.06$) and $7.8 \pm 6.2$ to $3.5 \pm 4.1$ points ($p = 0.004$), respectively; median CRP decrease-2.5 (IQR 0.8–4.8) to 0.45 (IQR 0.22–0.65) mg/dl ($p = 0.08$) and 1.5 (IQR 1.3–2.9) to 0.61 (IQR 0.5–1.1) mg/dl ($p = 0.005$), respectively; mean albumin increase - $4.1 \pm 0.5$ to $4.5 \pm 0$ mg/l ($p < 0.001$) and $3.8 \pm 0.53$ to $4.22 \pm 0.27$ mg/l ($p = 0.027$), respectively.
**Conclusion:** EEN is an effective therapeutic modality for active CD in adults. EEN therapy is associated with decreased clinical and biologic inflammatory activity, and may benefit patients with longstanding and newly diagnosed CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0327 COST PER CLINICAL OUTCOMES WITH VEDOLIZUMAB FOR THE TREATMENT OF MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS IN BRAZIL

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**Introduction:** Ulcerative colitis (UC) is a chronic condition associated with significant clinical and economic burden. Anti-tumour necrosis factor (anti-TNF) therapy has been shown to be effective in patients with UC refractory to conventional treatments. Recent research advances have led to the development of selective biologics targeting the gastrointestinal tract, such as vedolizumab (VDZ).
**Aims & Methods:** The aim of the study was to compare the cost per clinical outcomes of VDZ against infliximab (IFX) and adalimumab (ADA) for the treatment of anti-TNF-naive and anti-TNF-experienced patients with moderately to severely active UC from a private health care system perspective in Brazil. A systematic literature review identified randomized controlled trials (RCTs) for approved biologics up to February 2014. Outcomes of interest included sustained response and remission defined according to the Mayo score at 52 weeks, as reported in the individual RCTs. The treatment effect or the odds ratios with different biologics relative to placebo were estimated using Bayesian meta-analyses and were transformed into number-needed-to-treat (NNT) using the average placebo results across all trials. For the cost per outcomes analyses, it was assumed that responders to induction treatment with ADA and VDZ continued with maintenance treatment at 8 and 14 weeks respectively, based on the approved UC indication. For IFX, it was assumed that in the absence of response at 8 weeks, treatment was discontinued in line with RCT design. The time horizon was 52 weeks and no discounting was applied. Therapy costs, reported as Brazilian Real (R$), were calculated based on approved dose and frequency of administration; prices were obtained from the Brazilian official price list on 22 February 2016.
**Results:** At 52 weeks, the NNT and the cost per patient with sustained response and remission for anti-TNF-naive patients was estimated to be the lowest for VDZ versus IFX and ADA (Table 1). Among anti-TNF-experienced patients, the NNT for sustained response for VDZ and ADA was 5.1 (95% Confidence interval [CI]: 2.5–15.8) and 13.5 (4.9–80.9), respectively; and for sustained

**P0327: Table 1:** Number needed-to-treat (NNT) and cost per clinical outcomes of biologics among anti-TNF naive patients with UC.

| | Probability of induction response | | Probability of sustained response at 52 weeks | | NNT for sustained response at 52 weeks | | Cost (R$) per sustained responder at 52 weeks | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI |
| Placebo | 0.34 | (0.31; 0.37) | 0.12 | (0.09; 0.15) | Reference | | Reference | |
| Infliximab 5 mg/kg[1] | 0.69 | (0.62; 0.76) | 0.35 | (0.24; 0.47) | 4.4 | (2.9; 8.6) | 382,855 | (274,761;751,627) |
| Adalimumab 160/80/40 mg[2] | 0.49 | (0.41; 0.56) | 0.22 | (0.14; 0.32) | 10.2 | (5.0; 42.5) | 631,51 | (309,794;2,635,947) |
| Vedolizumab 300mg[3] | 0.63 | (0.51; 0.75) | 0.40 | (0.26; 0.55) | 3.6 | (2.2; 7.6) | 269,432 | (168,461;569,950) |
| | Probability of induction remission | | Probability of sustained remission at 52 weeks | | NNT for sustained remission at 52 weeks | | Cost (R$) per patient in sustained remission at 52 weeks | |
| | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI | Estimate | 95% CI |
| Placebo | 0.09 | (0.07; 0.11) | 0.04 | (0.03; 0.05) | Reference | | Reference | |
| Infliximab 5 mg/kg[1] | 0.34 | (0.27; 0.41) | 0.16 | (0.09; 0.25) | 8.4 | (4.8; 18.4) | 728,329 | (416,672;1,602,185) |
| Adalimumab 160/80/40 mg[2] | 0.17 | (0.13; 0.22) | 0.08 | (0.04; 0.14) | 22.3 | (9.7;101.2) | 1,384,105 | (603,505;6,284,048) |
| Vedolizumab 300mg[3] | 0.28 | (0.18; 0.40) | 0.19 | (0.11; 0.32) | 6.5 | (3.5;15.6) | 486,281 | (265,163;1,165,517) |

[1]infliximab 5 mg/kg induction treatment (week 0, 2, and 6) followed by every 8 weeks as maintenance treatment; [2]adalimumab 160 mg at week 0, 80 mg at week 2 for induction treatment followed by 40 mg every other week as maintenance treatment; [3]vedolizumab 300 mg induction treatment (week 0, 2, and 6) followed by every 8 weeks as maintenance treatment. Abbreviation: mg – milligrams; kg – kilograms; CI – Confidence intervals; NNT – Number needed-to-treat.

remission was 12.0 (4.8–44.5) and 39.2 (10.9- 283.1), respectively. The cost per sustained response for anti-TNF-experienced patients was lower with VDZ (R$ 322, 882; 95% CI: 160, 901-1, 002, 376) versus ADA (R$ 663, 415; 243, 006-3, 983, 940). Similarly, the cost per patient with sustained remission was R$ 760, 358 (95% CI: 302, 364-2, 826, 726) with VDZ and R$ 1, 928, 682 (95% CI: 537, 824-13, 943, 050) with ADA.

**Conclusion:** Compared to anti-TNF therapies, VDZ had the lowest NNT and cost per outcome, for both sustained response and remission at 52 weeks, among anti-TNF-naive and anti-TNF-experienced populations. The findings suggest VDZ potentially provides better clinical and economic value relative to anti-TNFs approved for the treatment of patients with moderately to severely active UC in Brazil.

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G. Muricy: Gabriela Muricyis is an employee of Takeda Pharmaceuticals International, Inc., São Paulo, Brazil.

H. patel: Haridarshan Patel is an employee of Immensity Consulting, Inc. which received funding for this project from Takeda Pharmaceuticals International, Inc.

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## P0328 DOSE ESCALATION OF BIOLOGICS IN CROHN'S DISEASE: CRITICAL REVIEW OF OBSERVATIONAL STUDIES

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**Introduction:** Biologics used to treat Crohn's disease (CD) may lose their effect over time, requiring dose escalation. While little information is available from randomized controlled trials, observational studies provide more evidence.

**Aims & Methods:** The aim was to summarize rates of dose escalation, its duration, responses and subsequent de-escalation in observational studies of CD in adults treated with adalimumab, infliximab, and vedolizumab in Europe. Two independent investigators conducted a systematic review, searching Medline and Embase for observational studies published 1998–2015 and proceedings from 4 major scientific meetings, including United European Gastroenterology Week, Digestive Disease Week, American College of Gastroenterology, European Crohn's and Colitis Organisation. Rates were summarized descriptively.

**Results:** In total, 62 articles from 12 European countries were analyzed (51 full articles and 11 abstracts), providing data from 8567 patients of whom 57% were females and 43% males. Thirty seven papers reported on 3899 patients with adalimumab and 34 papers on 4668 patients with infliximab. The male:female ratio was similar between drugs. No papers were located for vedolizumab. Overall, 28.4% (SD = 2.5%) of patients required dose escalation, including 30.2% (SD = 4.5%) with adalimumab and 26.0% (SD = 2.5%) with infliximab (P = 0.74). Rates increased according to line of treatment: 19% for first line, 37% second and 46% third. The median time to loss of response was 7 months; the weighted average time was 6.5 months. Average time to escalation was 6.6 (SD = 4.1) months; 6.5 months for adalimumab and 6.7 for infliximab (P = 0.497). Short-term response rates to escalation were 54% for adalimumab and 45% for infliximab (P = 0.97). Short-term remission rates were 53% for adalimumab and 49% for infliximab. Approximately 38% of patients were de-escalated. Few long-term data were available for analysis. Risk factors for loss of response included smoking, extensive resections and family history of inflammatory bowel disease. The risk was lower in TNF-naïve patients and in those receiving immunomodulators such as azathioprine. Other risk factors identified as associated with dose escalation were perianal disease, prior anti-TNF treatment, higher BMI, higher baseline CDAI, and stopping azathioprine.

**Conclusion:** A substantial proportion of patients receiving adalimumab or infliximab for Crohn's disease require dose escalation after a short period of time. Effective alternatives appear to be needed, especially for those who lose response and/or do not regain remission after escalation.

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## P0329 SELECTIVE GRANULOCYTE AND MONOCYTE APHERESIS IS EFFECTIVE AND SAFE IN GERIATRIC PATIENTS WITH ULCERATIVE COLITIS

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**Introduction:** Recently, the number of elderly patients with ulcerative colitis (UC) has increased in line with an increase in the number of patients developing UC. Additionally, treatment of elderly UC patients with conventional drugs, like salicylates, thiopurines, corticosteroids, or anti-cytokine biologics demands serious considerations of patients overall well-being, as immunosuppression may predispose to infection and other adverse effects. Granulocyte and monocyte apheresis (GMA) with an Adacolumn, if effective should be the treatment of choice in the elderly.

**Aims & Methods:** We were interested to evaluate efficacy and safety of the Adacolumn GMA in a geriatric setting. We retrospectively reviewed elderly and routine patients with moderate to severe UC, in whom remission was induced by GMA between April 2000 and January 2016. Any patient aged 65 years or more was regarded as an elderly, otherwise, he or she was classified as a routine patient. Of 95 patients who underwent GMA therapy in our hospital, 80 were eligible for inclusion, excluding those who had received GMA in combination with tacrolimus, prednisolone (PSL) or biologics. Lichtiger's clinical activity index (CAI) $\leq$4 meant clinical remission. To better understand the background factors, which potentially were associated with the response to GMA, we looked at gender, age at onset, duration of UC, UC location, baseline CAI, haemoglobin, albumin, C-reactive protein (CRP), estimated glomerular filtration rate (eGFR), Mayo endoscopic score and UCEIS, past PSL dose, presence of an underlying disease, drug-related complications.

**Results:** Clinical remission was achieved in 67 of the 80 patients, 78% for the geriatric group and an 85% for the routine group. Between the two groups, there were significant differences in the age at UC onset, UC duration, baseline CRP, eGFR, underlying disease, and PSL-related complications ($P < 0.05$). GMA-related transient headache was reported by 1 patient in each group, transient reduction in blood pressure and blood access failure were noted in 1 and 2 patients respectively in the elderly group, and heparin allergy in 1 patient in the routine group.

**Conclusion:** The clinical efficacy rates we achieved in these patients are very much higher than hitherto reported for GMA in UC patients, but very close to the published efficacy rates in steroid naïve patients. However, in the geriatric UC setting, drug therapy is more likely to cause adverse side effects as additional morbidity factors than in young patients. GMA monotherapy, as a non-pharmacological intervention appeared to be effective with good safety profile in all patients; a relevant option in geriatric setting.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### Reference

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## P0330 POSTOPERATIVE RECURRENCE OF CROHN'S DISEASE AND ITS ASSOCIATION WITH PLEXITIS

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**Introduction:** Surgery is not curative in Crohn's disease (CD), hence postoperative recurrence still remains significant problem. Currently conflicting data are available about the role of the clinical and the histological findings in CD postoperative relapse. However according to the latest data, presence of submucosal or myenteric plexitis can be predictive for postoperative relapse. We evaluated the frequency and predictors of postoperative recurrence and the role of the presence of submucosal and myenteric plexitis in predicting postoperative recurrence on the basis of endoscopic findings and/or the need for additional surgical resection.
**Aims & Methods:** Data from all patients who underwent CD-related resection at the University of Szeged, Hungary between 2004 and 2014 were analysed retrospectively. Demographic data, smoking habits, previous resection, treatment before and after the surgery, resection margins, neural fibre hyperplasia, submucosal and myenteric plexitis were evaluated as possible predictors on postoperative recurrence. Patients were controlled by colonoscopy regularly after surgery. Postoperative recurrence was defined on the basis of the endoscopic findings and/or the need of additional surgical resection.
**Results:** One hundred and four patients were included in the study. Ileocecal, colonic and small bowel resection were performed in 66.3%, 30.7% and 3% of the cases. Mean disease duration at the time of surgery was 6.25 years. Twenty-six patients underwent previous CD-related surgery. 43.2% of the patients was on 5-aminosalicylate, 20% on corticosteroid, 68.3% on immunomodulant and 4% on anti TNF-alpha postoperative treatment. Postoperative recurrence occurred in 63.5% of the patients, from them 92% relapsed within 5 years after the resection and second surgery was needed in 38% of the cases. Mean disease duration for endoscopic relapse was 2.19 years. The severity of submucosus plexitis was a predictor for the need of second surgery. Predictors for postoperative recurrence were also female gender (OR = 2.21, 95% CI 0.2–1.02, p = 0.056), penetrating disease behaviour (OR = 9.09, 95% CI 0.01–1.09, p = 0.06) and isolated ileal localisation (OR = 6.41, 95% CI 0.024–1.0, p = 0.05). No association was revealed between postoperative recurrence and smoking status, postoperative prophylactic treatment and the presence of myenteric plexitis and relapse.
**Conclusion:** Severity of submucosus plexitis, penetrating behaviour and isolated ileal localisation proved to be predictors of postoperative recurrence of CD. Our results did not confirm the hypothesis about the predictive role of myenteric plexitis in postoperative relapse.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0331 RELATED RISK FACTORS ASSOCIATED WITH STEROID RESISTANCE IN AN IRISH IBD POPULATION

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**Introduction:** Glucocorticoids (GCS) remain the gold standard for treating an acute flare of IBD & response rates are often unpredictable. Resistance rates have been estimated to range from 20–30%, however related or predictive factors associated with GCS resistance remain uncertain.
**Aims & Methods:** To estimate local steroid resistance rates amongst an Irish IBD cohort & to identify related risk factors driving resistance. **Methods:** A retrospective review of patients from HIPE data requiring hospitalisation for an acute flare of colitis from 2010–2015 was undertaken. Demographics & clinical details including phenotype, behaviour, severity, duration, therapies, CRP, rates of hypoalbuminaemia (albumin < 35 g/dl), rates of anaemia (hb < 10.5 g/l), length of stay (LOS) were all recorded. Resistance rates were determined by a lack of improvement or deterioration in day 3 CRP or a need for therapy escalation or surgery. Steroid dependence was defined as a relapse of symptoms within 3 months of stopping IV GCS. Results were compared amongst responders & non-responders using a student t-test and p value of $<0.05$ was considered significant.
**Results:** In all 473 patients requiring hospitalisation for acute colitis were identified, of which we have analysed data on 247 patients to date. A total of 74 (29%) of the 247 patients were excluded due to insufficient information. Of the remaining 173, 99 (57%) were female, mean age was 39yrs (range15–84yrs), mean disease duration was 4.5yrs (range 0–27yrs). There were statistically more patients with Crohn's disease (CD) 98 (57%) than UC 75 (43%), p = 0.009, 95% CI 0.03 to 0.24. In all 52 (30%) had severe, 87 moderate (50%), 36 mild (20%) disease. Overall the mean LOS was 10 days (range 3–49) and admission CRP 59 mg/l (range 1–307.9 mg/l). Mean day 3 CRP was 25 mg/l (range 1–260 mg/l). In all, 103 (60%) were responders, 55 (31%) were steroid resistant & 15 (9%) were steroid dependent. Overall resistant patients had more severe disease vs. responders 25 (45%) vs. 17 (17%), $p < 0.0001$, OR 4.2, 95% CI 2.00 to 8.86. Mean CRP on day 3 for responders and non-responders was 10 mg/l vs. 48 mg/l. CRP > 45 mg/l on day 3 appeared to be predictive of steroid resistance, OR 20.6, 95% CI 5.78–73.37, $p < 0.001$. Overall resistant patients had higher rates of anaemia (24%, n = 13, vs 13%, 13) and hypoalbuminaemia (29%, n = 16 vs. 23%, n = 24) on admission and on day 3 of admission ((36%, n = 20 vs 19%, n = 20 and 55%, n = 30 vs. 34%, n = 35 respectively), however day 3 hb (OR 0.42, $p \leq 0.02$ 95% CI 0.2–0.9)) and albumin (OR 0.42, $p \leq 0.01$, 95% CI 0.2–0.8) appeared to be predictive of response. Overall disease subtype, concomitant therapies or disease extent did not appear to influence resistance rates, however amongst UC patients pancolitic patients had higher resistance rates, n = 21 (28%) vs. n = 8 (7%), $p < 0.0001$, 95%CI 0.18–0.42. In all 44 (80%) of the resistant patients required surgical intervention, of which 13 (30%) had failed rescue biologic therapy.
**Conclusion:** GCS resistance rates in our cohort are similar to previously published figures and significant at 31%. A high CRP, anaemia, hypoalbuminaemia on day 3 as well as severe disease & pancolitis are predictive of GCS resistance. Further work on mechanisms of steroid resistance is needed as most required surgery and did not respond to a biologic.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0332 THE INCIDENCE OF SUBOPTIMAL THERAPY AFTER INITIATING A SECOND TUMOUR NECROSIS FACTOR ANTAGONIST IN PATIENTS WITH CROHN'S DISEASE: A MULTI-COUNTRY CHART REVIEW

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**Introduction:**Patients with Crohn's disease (CD) treated with tumour necrosis factor antagonists (anti-TNF) may require treatment modifications (i.e., dose escalation, switch to another anti-TNF, surgery, or addition of other medications). Such changes can be used as surrogate of loss of response and may be considered as indicators of suboptimal therapy.
**Aims & Methods:** Our aim was to evaluate the incidence of indicators of suboptimal therapy among adult patients with CD treated with a second anti-TNF using data from real-world clinical practices. A retrospective chart review study conducted in six countries (Canada, France, Germany, Italy, UK, and Spain) recruited CD patients initiating anti-TNF therapy between June 2009-2011. We measured the incidence of suboptimal therapy over two years and time to the first indicator of suboptimal therapy among patients who switched from initial anti-TNF to a second anti-TNF. Indicators of suboptimal therapy with a second anti-TNF included anti-TNF dose escalation (assessed >4 months after index to allow for initial dose optimization), augmentation with aminosalicylates, immunomodulators, or corticosteroids, discontinuation of anti-TNF therapy, switching to another anti-TNF, and CD-related surgery. Time to the first occurrence of the indicator of suboptimal therapy was measured using the Kaplan-Meier Method, where patients were censored after discontinuation of therapy or at the end of the follow-up period.
**Results:** The study included a total of 657 anti-TNF naÿve CD patients of which 174 (26.5%) initiated a second anti-TNF during follow up [mean age (SD): 38.8 (13.3) years, 37.9% females]. Median duration of CD was 7.7 years and with first anti-TNF therapy was 12.3 months. Among patients with reported physician global assessment score (n = 123), 76.4% had moderate to severe CD. 70.1% of patients had an ongoing treatment with at least one non-biologic therapy at the time of initiation of the second anti-TNF therapy. The percentage of patients on adalimumab and infliximab as the second anti-TNF therapy was 63.2% and 36.8% respectively. Fifty-six percent of patients had at least one indicator of suboptimal therapy within two years after initiating a second anti-TNF therapy. Discontinuation (29.9%), dose escalation (16.7%) and augmentation (16.7%) were the most frequently reported indicators of suboptimal therapy. Median time to at least one of the indicators of suboptimal therapy was 13.0 months (95% CI: 10.1 - 19.8).
**Conclusion:** Over half of CD patients treated with a second anti-TNF therapy experienced at least one indicator of suboptimal therapy within 2 years of therapy. The most common indicators were discontinuation and dose escalation with anti-TNFs and augmentation with non-biologic therapies. Future research should determine the potential for alternative therapies to improve treatment response rates among patients who experience loss of response with anti-TNF therapies.
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## P0333 REAL-WORLD CHARACTERISTICS OF THE FIRST USERS OF VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE PATIENTS IN ISRAEL

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**Introduction:** To describe the real-world characteristics of patients with moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD) who initiated vedolizumab (VDZ) in Israel in 2015.
**Aims & Methods:** A retrospective cohort study was performed using the computerized databases of Maccabi Healthcare Services (MHS), a 2-million-member healthcare maintenance organization representing 25% of the Israeli population. Patients with at least one dispensed prescription of VDZ in the year 2015 were included. They were classified as having UC or CD based on the last gastroenterologist diagnosis prior to treatment initiation (index). Socio-demographic and clinical characteristics were described at index, including a Deyo-Charlson comorbidity index (CCI) augmented with the MHS chronic disease registries. Baseline annual healthcare resource utilization was measured by physician visits, hospitalization and laboratory data.
**Results:** In 2015, a total of 95 patients with UC (n = 37, 39%) or CD (n = 58, 61%) initiated VDZ. The mean age (SD) of UC (56% female) and CD patients (55.2% female) was 37.0 (16.1) and 36.3 (15.1) years, respectively. The median (IQR) disease duration before VDZ initiation was 6.0 (10.1) and 9.1 (7.3) years for UC or CD patients, respectively. Among recently diagnosed (2010–2015) VDZ initiators, over two-thirds had started their initial UC or CD treatment with 5-aminosalycylates (5-ASA) and 85% were experienced with other biological therapies. Overall, a third of patients were overweight or obese and 6.3% were diabetic. The mean (SD) CCI was 0.92 (1.19) and 0.84 (1.18) for UC and CD patients, respectively. In the year prior to VDZ initiation, 30% of patients had seen a gastroenterologist more than 4 times and 38% had been hospitalized.
**Conclusion:** In the first year of licensure in Israel, results indicate that uptake of VDZ was amongst primarily anti-TNF experienced patients experiencing significant health care resource utilization. Real-world evidence on patient characteristics will inform planned studies of treatment patterns and outcomes of VDZ treatment, including longer-term comparative effectiveness and safety studies to allow assessment of appropriate place of VDZ in therapy.
**Disclosure of Interest:** C. Weil: CW is an employee of Maccabi Health Services Israel and conducted the study with funding from Takeda Pharmaceuticals.
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## P0334 POOR TOLERABILITY PROFILE OF THIOPURINES IN INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE SINGLE-CENTRE EXPERIENCE

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**Introduction:** In inflammatory bowel disease (IBD) treated with thiopurines, the occurrence of adverse events (AEs) leading to discontinuation of the drug is reported in 10% to 28% of patients. However, the majority of the studies on this topic were retrospective and primarily designed to assess efficacy of thiopurines, but not safety.
**Aims & Methods:** The aim of this study was to evaluate thiopurine tolerability in patients with IBD in a real-life setting, and the factors associated with the occurrence of AEs leading to treatment withdrawal. This study was conducted at the Division of Internal Medicine of "Villa Sofia-Cervello Hospital", Palermo, a tertiary referral centre for IBD. Data collection was performed as part of a post-marketing surveillance project on the AEs of immunosuppressants and biologics granted by the Italian Medicines Agency (AIFA). All consecutive patients who started a treatment with azathioprine (AZA) from January 2010 to March 2016 were entered in a prospectively maintained database. All AEs which led to the permanent discontinuation of the drug were reported. Switch to 6-mercaptopurine (6-MP) and its related outcomes were also recorded. All variables at baseline were assessed at univariate analysis in order to identify predictive factors of AEs.
**Results:** 253 patients were included. Mean age was 40.4 years, the majority of patients were males (60.1%) and affected by Crohn's Disease (64.4%). The median total follow-up was 32 months (range: 0.2–75 months). At the end of the study, AZA was discontinued in 160 patients (63.2%). The main reason leading to drug withdrawal was the occurrence of AEs (109/160 patients [68.1%]; cumulative incidence among the entire cohort: 43.1%); in 47/160 patients (29.4%), AZA was stopped due to inefficacy, and in 3/160 patients (1.9%) after a sustained clinical remission. In two patients, discontinuation of therapy was arbitrary. Overall, the most frequent AEs leading to treatment withdrawal were nausea and/or vomit (31/253 patients, 12.3%) and subjective symptoms, i.e. nonspecific and poorly defined side effects such as fatigue, headache, and muscle pain (20/253 patients, 7.9%) (Table 1). Among the 109 patients who discontinued AZA due to AEs, an attempt to restart a thiopurine-based treatment using 6-MP was performed in 44 cases (40.4%). At the end of the follow-up, 6-MP was discontinued in 35/44 patients (79.5%), mostly due to AEs (29/35 patients, 82.8%), which were the same of those reported during treatment with AZA in nearly half of the cases. At univariate analysis, AZA-induced hepatic and pancreatic toxicity were associated with male gender ($p = 0.01$, and $p = 0.03$, respectively), occurrence of nausea with Crohn's disease ($p = 0.04$), and the concomitant use of proton pump inhibitors with the absence of development of subjective symptoms ($p = 0.04$).

| Adverse event | Cumulative Incidence, n (%) |
|---|---|
| Nausea Subjective symptoms Hepatotoxicity Pancreatic toxicity Flu-Like syndrome Leucopenia Cutaneous reactions Bone marrow failure Infections Cancer | 31 (12.3%) 20 (7.9%) 14 (5.5%) 13 (5.1%) 12 (4.7%) 6 (2.4%) 6 (2.4%) 4 (1.4%) 2 (0.8%) 1 (0.4%) |
| **Total** | **109/253 (43.1%)** |

**Conclusion:** In a real-life setting, the tolerability profile of thiopurines is poor, with a very high rate of discontinuation of therapy due to AEs.
**Disclosure of Interest:** A. Orlando: served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals and received lecture grants for AbbVie, MSD, Sofar, Chiesi, and Takeda Pharmaceuticals.
All other authors have declared no conflicts of interest.

## P0335 PROGNOSTIC VALUE OF THE MAGNITUDE OF CYTOMEGALOVIRUS REACTIVATION EVALUATED BY IMMUNOHISTOCHEMICAL STAINING IN PATIENTS WITH ULCERATIVE COLITIS

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**Introduction:** Cytomegalovirus (CMV) reactivation in the colon has been involved in steroid refractoriness in patients with ulcerative colitis (UC). Its diagnosis is based on the detection of CMV by means of specific immunohistochemistry (IHC) or PCR on rectal biopsies. Although the benefit of antiviral therapy in this clinical setting is still under debate, a threshold of CMV copies by PCR has been associated with a poorer outcome.
**Aims & Methods: Aim:** To assess whether the intensity of CMV reactivation measured by the number of positive cells by IHC, is associated with the short-term prognosis in these patients. **Methods:** UC patients with IHC-CMV+ were identified in three different hospitals. The biopsies were reviewed by expert pathologist and the maximum number of cell IHQ-CMV+ in each biopsy sample was determined. Baseline and evolutive clinical variables were recorded.
**Results:** We included 48 patients, with a median age of 40 years (IQR 32-55). 67% had extensive UC, 25% presented severe activity and the median time of UC duration at the index flare was 26 months (IQR 2-73). At the moment of

**P0337: Table 1:** Characteristics of patients presenting with LGIB.

| | Acute admissions N = 2331 N (%) | Inpatients N = 185 N (%) | All patients § Total N = 2528 N (%) |
|---|---|---|---|
| **Median Age** (IQR) | 73 (56-83) | 78 (66-85) | 74 (57-83) |
| **Charlson Co-morbidity index** 0 1 ≥ 2 (Missing) | 1016 (43.6) 530 (22.6) 778 (33.8) 7 | 42 (22.7) 39 (21.1) 104 (55.2) 0 | 1066 (42.2) 570 (22.6) 885 (35.2) 7 |
| **Drugs** Aspirin Warfarin Direct Oral Anticoagulants (Missing) | 532 (22.8) 247 (10.6) 122 (5.2) 1 | 51 (27.5) 21 (11.3) 7 (3.8) 11 | 584 (23.1) 270 (10.7) 131 (5.2) 18 |
| **Shocked*** (Missing) | 48 (2.1) 64 | 9 (4.9) 13 | 58 (2.3) 75 |
| **Admitting Hb** Median (IQR) (Missing data) | 124 (101-139) 5 | 107 (88-124) 1 | 122 (100 -139) 14 |
| **Mortality** (Missing data) | 51 (2.2) 34 | 33 (17.9) 1 | 85 (3.4) 36 |

§Includes 12 patients classified as 'other' and 2 with missing data. *On admission or first set of observations after developing LGIB. Shock defined as HR ≥ 100 and SBP < 100 mmHg.

CMV reactivation, 70% were receiving corticosteroids, 22% azathioprine, and 19% antiTNF agents. The median number of IHC-CMV+ cells were 2 cells/biopsy (IQR 1-5). No factors were associated with the magnitude of the reactivation. Thirty-two patients (67%) were treated with antiviral therapy. Thirteeen patients (27%) underwent colectomy; persistence of CMV was reported in 6/13 (46%) of the surgical specimens. The colectomy during admission for the index flare was significantly higher in patients with >2 cells/biopsy (50% vs. 16%, p = 0.022) and in patients with more severe activity (58% vs. 19%, p = 0.01).
**Conclusion:** The intensity of CMV colonic reactivation in patients with refractory UC, as measured by IHC, could be of prognostic relevance. Our data, together with a previous rectal PCR study, suggest that the decision to start antiviral treatment might rely on the quantitative measure of CMV reactivation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0336 FIVE YEAR BUDGET IMPACT ANALYSIS OF BIOSIMILAR INFLIXIMAB (CT-P13) FOR THE TREATMENT OF CROHN'S DISEASE AND ULCERATIVE COLITIS IN SPAIN

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**Introduction:** Crohn's disease (CD) and ulcerative colitis (UC) are immune-related diseases that are particularly common in the European population. Treatment with biologic drugs such as infliximab may be suitable for many patients with these diseases; however, these drugs are usually expensive and therefore access to treatment is often restricted. Biosimilar infliximab (CT-P13) has a lower cost than the infliximab reference product (RP) and has been approved for use in CD and UC in Europe, the USA and elsewhere.
**Aims & Methods:** The aim of this study was to analyse the pharmacoeconomic effects of the use of biosimilar infliximab in CD and UC in Spain. An Excel-based model was developed to apply three different price-discount scenarios (20%, 30%, and 40% discount versus RP) and to evaluate potential cost savings in Spain over five years. Total population, disease prevalence and incidence, annual prevalent population receiving RP and the public price of RP in Spain were parameters used in the model. To calculate the maximum possible cost savings associated with use of biosimilar infliximab, the analysis presumed that all RP-treated patients in Spain would switch to biosimilar infliximab.
**Results:** After applying the 20%, 30%, and 40% price-discount scenarios to the CD population, cumulative cost savings over five years were €223, 295, 625, €373, 550, 625, and €446, 591, 250, respectively. With these savings, an additional 7, 605, 15, 289, and 20, 265 CD patients, respectively, could be treated using biosimilar infliximab annually. In the UC population, total cost savings over five years with the 20%, 30% and 40% price-discount scenarios were estimated to be €247, 068, 522, €371, 431, 872, and €493, 952, 802, respectively. With these savings, an additional 8, 415, 15, 202 and 22, 414 patients with UC could access biosimilar infliximab treatment each year.
**Conclusion:** Cost savings in this study were calculated assuming that all patients being treated with RP were switched to biosimilar infliximab. Applying this assumption, this study showed that biosimilar infliximab use in CD and UC could result in significant cost savings compared with RP use. Savings generated via the use of biosimilar infliximab could help ease the economic burden of CD and UC treatment and/or allow more patients to access biologic therapy.
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### P0337 OUTCOMES OF ACUTE LOWER GASTROINTESTINAL BLEEDING: DATA FROM A LARGE NATIONWIDE AUDIT

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**Introduction:** Lower gastrointestinal bleeding (LGIB) is a common indication for emergency hospitalisation. There are few data characterising its modern day epidemiology, interventions and outcomes. This study describes characteristics, aetiology and management of patients admitted to UK hospitals with LGIB.
**Aims & Methods:** Prospective national audit of consecutive presentations with LGIB from September to December 2015 in acute hospitals in the UK. Data were collected on demographics, transfusion, investigations, interventions and outcome. Cases were identified by clinical teams and data entered into a centralised website until discharge or 28 days.
**Results:** 2528 cases of LGIB were identified across 138 hospitals. Median age 74 (57–83), 1319 (52.5%) female. 1994/2521 (79.1%) patients had co-morbidities, e.g. hypertension (39.8%), diabetes (15.0%) and chronic respiratory disease (11.8%). 1075/2510 (42.8%) patients were receiving an oral anti-platelet or anticoagulant. Inpatients accounted for 185/2405 (7.3%) bleeds. Shock and anaemia were infrequent, but more common in inpatients (table 1). 666/2493 (26.7%) patients received a red cell transfusion, 258/2493 (10.3%) requiring more than 4 units. 642/2481 (25.9%) had flexible sigmoidoscopy or colonoscopy whilst admitted and 54/2450 (2.2%) received endoscopic haemostasis. 507/2452 (20.7%) underwent computed tomography (CT) of the abdomen, 149/2452 (6.1%) CT angiography, 37/2467 (1.5%) mesenteric angiography and 19/2504 (0.8%) embolization. 1213/2473 (49.0%) had no inpatient investigations. 6/2475 (0.4%) underwent laparotomy for bleeding and 5/2475 underwent transanal surgery for bleeding. 260/1993 (13.0%) were re-admitted within 28 days, 111/1993 (5.6%) due to further LGIB. Death at 30 days was 85/2492 (3.4%). The most frequent discharge diagnoses were diverticular disease (668/2528, 27.1%), benign anorectal conditions (422/2528, 17.1%) and source unidentified (576/2528, 23.4%).
**Conclusion:** LGIB is a disease of older patients, diverticular disease is the most common aetiology and a quarter receive red cell transfusion. Half of presentations had no in-patient investigations. When flexible sigmoidoscopy, colonoscopy and CT are used, they rarely lead to endoscopic haemostasis or mesenteric embolization. Surgery is rarely required and case fatality rates are low.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0338 STIGMATA OF RECENT HEMORRHAGE AND NON-ASPIRIN ANTIPLATELET DRUG ARE PREDICTIVE FACTORS FOR REFRACTORY COLONIC DIVERTICULAR HEMORRHAGE

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**Introduction:** Colonic diverticular hemorrhage is usually self-limited but is often recurrent. In some cases, radiological intervention or operation is required due to repeated rebleeding. In the present study, we investigated predictive factors for the rebleeding of colonic diverticular hemorrhage.
**Aims & Methods:** We studied 474 episodes (290 patients) of colonic diverticular hemorrhage from January 2006 to February 2016 in our hospital. The diagnosis of colonic diverticular hemorrhage was based on all of the following findings; 1. hematochezia without abdominal pain, 2. diverticulosis confirmed by colonoscopy or computed tomography, and 3. no other cause of hematochezia. Stigmata of recent hemorrhage were defined as active bleeding, non-bleeding visible vessel, or adherent clot in the diveluticulum at colonoscopy. When we found them, endoscopic hemostasis was performed. Rebleeding was defined as hematochezia requiring colonoscopy. Early and late bleeding were defined as

rebleeding within 1 week and 2–4 weeks after the first colonoscopy, respectively. In the analysis of late rebleeding, 3 episodes were excluded because hemicolectomy was performed due to rebleeding within 1 week. Using multivariate logistic regression, we analyzed the following factors to identify predictive factors for the rebleeding: age, sex, shock vital on admission, comorbidities (hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease, cerebrovascular disease, chronic liver disease, hemodialysis), current medication (low-dose aspirin, non-aspirin antiplatelet drug, anticoagulants, non-steroidal anti-inflammatory drug, corticosteroid), extravasation confirmed by contrast enhanced computed tomography, identification of bleeding spot, and stigmata of recent hemorrhage.
**Results:** Stigmata of recent hemorrhage were identified in 128 (27%) episodes including 105 active bleeding. Endoscopic hemostasis was performed in all of these episodes; clipping was used in most cases (117, 90.7%). Early and late rebleeding were observed in 59 (12.4%) and 28 (6%) episodes. Stigmata of recent hemorrhage (odds ratio, 2.30; 95% confidence interval, 1.30–4.05, $p = 0.0072$) and non-aspirin antiplatelet drug users (odds ratio, 2.42; 95% confidence interval, 1.06–5.52, $p = 0.035$) were identified as significant and independent predictive factors for early and late rebleeding, respectively. In the subgroup analysis of 117 episodes with endoscopic clipping, early rebleeding occurred more often in the diveluticulum located in the left side of the colon (14/42, 33.3%) than that in the right side (10/75, 13.3%) (odds ratio, 3.07; 95% confidence interval, 1.20–7.87, $p = 0.02$).
**Conclusion:** Stigmata of recent hemorrhage were predictive factor for early rebleeding even after endoscopic hemostasis. Endoscopic clipping may not be effective enough for the management of colonic diverticular hemorrhage especially in the left side of the colon. We should be alert to late rebleeding in non-aspirin antiplatelet drug users.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0339 COMPARISON OF CT, SIGMOIDOSCOPY AND COLONOSCOPY AS INITIAL METHODS OF EXAMINATION FOR PRESENCE OF HEMATOCHEZIA

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**Introduction:** The preferred method of examination of hematochezia is sigmoidoscopy and colonoscopy; However, in cases of emergencies, the bowel preparation can be poor and entry to the upper level is very difficult. On the other hand, computed tomography offer a non-invasive way to evaluate both enteric and extra enteric abnormalities. It is also efficient in verifying the point of hemorrhage.
**Aims & Methods:** The purpose of this research is to compare whether computed tomography are no more inferior than sigmoidoscopy and colonoscopy as the initial method of examination in patients who have sought medical assistance because of the presence of hematochezia. Medical records dating from January 2012 to March 2015 were retrospectively analyzed for 279 adult patients over 18 years of age who had sought medical attention and undergone computed tomography (CT), sigmoidoscopy, or colonoscopy as a result of the presence of hematochezia. Patients with hematochezia were divided into groups who underwent initial examinations via computed tomography, sigmoidoscopy, and colonoscopy. The data presents a comparison of each group by the detection rate of bleeding focus, through initial inspection, hospital stay, and period until the final diagnosis.
**Results:** Of the 279 enrolled patients with hematochezia, 91 underwent sigmoidoscopy, 58 underwent colonoscopy, and 130 initially underwent computed tomography. There were no significant differences in the figures of patients in each group when comparing the early detection rate of bleeding focus and hospital stay ($p = 0.491$). With the exception of 39 patients whose bleeding focus could not be determined through examination, there were no significant differences in the length of time required to obtain a final diagnosis when comparing the 240 target patients in each group ($p = 0.258$). In the CT treatment group, 125 patients (96.2%) subsequently underwent endoscopy. In the case of those who underwent endoscopic therapy, 15 patients (11.5%) were from the CT treatment group, and 36 (24.2%) were those who had initially undergone sigmoidoscopy and colonoscopy ($p = 0.007$). Of the CT treatment group, there were 9 patients (6.9%) who experienced extravasation, while among those who did not have extravasation, there was 1 patient (0.8%) who experienced significant bleeding (Hemoglobin $\leq 6$ g/dL, systolic blood pressure $\leq 90$ mmHg).
**Conclusion:** This study showed that CT as an initial inspection of patients with hematochezia showed no significant differences in figures related to the duration of diagnostics through initial inspection, hospital stay, and length of time required to obtain a final diagnosis when compared to patients who underwent sigmoidoscopy and colonoscopy. There were significantly more patients who underwent endoscopic therapy from the sigmoidoscopy and colonoscopy groups than from the CT group. The results suggest that CTs might be considered an alternative to sigmoidoscopy when initializing exams related to hematochezia.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0340 ENDOCLOTTM PROPHYLAXIS FOLLOWING COMPLEX ENDOSCOPIC RESECTION OF GASTROINTESTINAL NEOPLASIA: NO NEED TO BLEED!

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**Introduction:** EMR / ESD of large lesions creates large mucosal defects and is associated with significant post-procedural bleeding. Endoclot™ is a topical hemostatic powder that rapidly absorbs water creating a high concentration of platelets, red blood cells and clotting factors – accelerating the natural coagulation cascade.
**Aims & Methods:** Routine application of Endoclot™ to ESD or EMR defects is hypothesised to reduce the risk of significant post EMR/ESD bleeding. A prospective registry was set up to record all EMR / ESD procedures since 2006. Prophylactic use of Endoclot™, following endoscopic resection of lesions $> 20$ mm, to prevent delayed bleeding was introduced in June 2014. The bleeding rate since the introduction of this strategy was compared with the bleed rate of our historic cohort since 2006. Bleeding was defined as significant if it required: readmission, transfusion or further intervention. SPSS was used for statistical analysis of data.
**Results:** Pre-Endoclot cohort: 496 patients underwent lower gastrointestinal EMR/ESD at our institution between 2006 and 2013 with a mean polyp size of 43 mm and 12% of these polyps were scarred due to previous intervention. Significant delayed bleeding was seen in 21/496 patients (4%). 264 patients underwent upper gastrointestinal EMR/ESD at our institution between 2006 and 2013. Significant delayed bleeding was seen in 9/264 patients (3%). Endoclot cohort: 71 patients have undergone colonic EMR/ESD (mean polyp size 46 mm, 38% scarred) (Table 1). 61 patients have undergone upper gastrointestinal resection (mean lesion size 33 mm, 37% scarred).
There was 1 significant delayed bleed in the colonic group (1%) requiring further endoscopic therapy. There were 2 bleeds (3%) in the upper GI group, which were managed with further endoscopic therapy without the need for blood transfusion. There have been no complications related to Endoclot™ use. Device clogging was experienced in 5% of upper gastrointestinal cases and 15% of lower gastrointestinal cases.

**Table 1:** Colonic ER Outcomes.

| | Mean Lesion Size (mm) | Scarring % | Delayed Bleeding % |
|---|---|---|---|
| Pre-Endoclot n = 496 | 43 | 12 | 4 |
| Post-Endoclot n = 71 | 46 | 38 | 1 |
| P-value | NS | <0.01 | NS |

**Conclusion:** Endoclot™ shows promise in reducing the risks of delayed bleeding following endoscopic resection of large neoplastic lesions from the gastrointestinal tract. Our data demonstrates a 75% reduction in risk of delayed bleeding following EMR/ESD for large colonic polyps in a group with a significantly higher rate of scarring and therefore bleeding risk. A randomised controlled trial is required to clarify the role of routine use of Endoclot™ following EMR/ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0341 RISK FACTORS FOR ACTIVE BLEEDING FROM COLONIC ANGIODYSPLASIA CONFIRMED UNDER COLONOSOCPIC OBSERVATION

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**Introduction:** Colonic angiodysplasia is an important cause of lower gastrointestinal bleeding in the elderly, but there have been few studies on its risk factors for bleeding. Thus, we retrospectively investigated the risk factors for bleeding from colonic angiodysplasia which was confirmed under colonosocopic observation.
**Aims & Methods:** Among 24334 patients who underwent colonoscopic examination from 2006 November to 2015 November in our hospital, 435 patients with colonic angiodysplasia were studied. The following factors were analyzed to identify risk factors for active bleeding from colonic angiodysplasia at the time of colonoscopy: age, sex, co-morbidities (heart disease, liver cirrhosis, chronic kidney disease, chronic obstructive pulmonary disease, and diabetes mellitus), medications (antiplatelet drugs, anticoagulants, and non-steroidal inflammatory drugs) and endoscopic features of colonic angiodysplasia.

**Results:** Among the 435 patients with colonic angiodysplasia, active bleeding from the angiodysplasia was observed in 29 patients (6.7%). Using multivariate logistic regression analysis, we identified the following factors as independent and significant risk factors for the bleeding: age over 80 years (odds ratio (OR), 5.2; 95% confidence interval (CI), 1.6–16.5), heart disease (OR, 6.9; 95%CI, 1.04–45.5), use of anticoagulants (OR, 4.2; 95%CI, 1.2–14.9), multiple angiodysplasia (OR, 6.7; 95%CI, 1.8–25.2) and small angiodysplasia less than 5 mm (OR, 17.7; 95%CI, 4.9–64.0). With regard to characteristics of angiodysplasia, colonic angiodysplasia with active bleeding was mostly located in the right colon (90%, 26/29) and 1–2 mm in size (83%, 24/29). All patients with active bleeding from colonic angiodysplasia were successfully treated with endoscopic clipping or argon plasma coagulation. Rebleeding occurred in 9 patients (31%, 9/29) during follow-up period of a median of 16 months ranging 2–84 months. No patient required angiographic embolization, hormonal therapy or surgical resection.
**Conclusion:** Multiple or small colonic angiodysplasias in patients of advanced age, with heart disease, or under use of anticoagulants have an increased risk for bleeding. We should be alert to small colonic angiodysplasia in the right colon at colonoscopy and consider prophylactic treatment for bleeding in patients with those risk factors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0342 PREVENTING DELAYED POST-POLYPECTOMY INDUCED ULCER HEMORRHAGE BY USING DOPPLER ENDOSCOPIC PROBE AS A GUIDE TO RISK STRATIFICATION & PROPHYLACTIC HEMOSTASIS AFTER POLYPECTOMY

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**Introduction:** Delayed post-polypectomy ulcer (PPIU) bleeding is increasing in prevalence as more colorectal cancer screening is performed and large polyps are removed. A recently published large retrospective report recommended hemoclip (HC) closure of all PPIUs during screening colonoscopy of high risk patients to prevent severe delayed bleeding[1]. However, this approach may not be effective because: 1) HC closure of PPIUs > 15 mm is usually not possible with current HCs 2) a large number of HCs is required for closure of large PPIUs or multiple PPIUs in the same patient & 3) this technique covers up rather than obliterates underlying arteries which later are exposed after the HCs come off. We hypothesized that the underlying vessels in PPIUs could be localized & focally treated after polypectomy with Doppler endoscopic probe (DEP) guidance to prevent and effectively prevent delayed PPIU hemorrhage.
**Aims & Methods:** 1) to determine the prevalence of blood flow by DEP in PPIUs just after colon polypectomy, 2) in an initial cohort, to utilize DEP for risk stratification and to determine the natural history of untreated PPIUs with positive DEP, 3) in a second cohort to use DEP as a guide for focal hemostasis to obliterate the underlying blood flow, & 4) to report 30 day rates of bleeding & complications in both cohorts. In two consecutive prospective cohort studies, 62 outpatients having elective screening or surveillance colonoscopies were included. Standard colon preps & techniques for removal of benign appearing pedunculated or sessile polyps were used. Sizes of the PPIUs were estimated with accessories of known dimensions. After polypectomy, a disposable colon DEP (Vascular Technology Inc, Nashua, NH) was used to interrogate the PPIUs for superficial (<4 mm) blood flow (both arterial & venous) & to map the vessel course. The first cohort of 30 patients did not have prophylactic hemostasis and the second cohort of 32 patients with arteries detected in the PPIUs had hemostasis (HC or MPEC) until arterial blood flow was obliterated. ASGE guidelines for anti-coagulants & anti-platelet drugs were followed before & after colonoscopy.
**Results:** Patients in the 2 cohorts had similar risk factors for delayed PPIU bleeding. 30 of the 62 patients (48.4%) had arterial blood flow detected in 1 or more PPIUs with DEP - none was venous. None had visible arteries or stigmata of hemorrhage. For 120 polyps removed (range 1- 5 /patient), PPIUs were 6 – 30 mm & 37 PPIUs (30.8%) had arterial flow detected. For PPIUs < 10 mm only 3/37 (8%) had + DEP, for 10–14 mm PPIUs 15/53 (28.3%) had + DEP, & for PPIUs 15 mm or larger, 19/30 (63.5%) had + DEP, that were focal in the PPIUs & usually short in course. For the initial 30 patients not treated with hemostasis, the delayed bleeding rate was 16.7% (5/30). For the next 32 patients treated with DEP guided hemostasis, the delayed bleed rate was 0% (0/32). No other complications occurred.
**Conclusion:** 1) DEP facilitated mapping of artery location & blood flow in PPIUs. 2) Arterial blood flow was detected in increasing prevalence from < 8% in PPIUs < 10 mm; to 28% for PPIUs 10 - 14 mm in diameter; to 63% of PPIUs 15 mm or larger. 3) With focal treatment of arteries in the base of PPIUs & obliteration of blood flow as monitored by DEP, no patient had delayed PPIU bleeding. 4) In contrast 16.7% of those not treated endoscopically had delayed bleeding from PPIUs and all had positive blood flow at baseline. Disclosures – Funding. Supported in part by a VA Clinical Merit Review Research Grant and CURE DDRC NIH 41301 (Human Studies Core).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0344 A RISK ANALYSIS OF POSTPOLYPECTOMY BLEEDING IN COLONOSCOPY DUE TO A COMBINATION OF ANTITHROMBOTIC AGENTS

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**Introduction:** Postpolypectomy bleeding (PPB) is a major complication of colorectal polypectomy and antithrombotic agents are one of the major risk factors for PPB. PPB risks have been reported for each kinds of antithrombotic and several guidelines have been published regarding possible management modalities. However, little is known about PPB risks in patients taking multiple antithrombotics. Therefore, we investigated PPB risks with regard to the use of multiple antithrombotics.
**Aims & Methods:** A total of 6, 387 colonoscopies involving polypectomy (endoscopic mucosal resection [EMR] / cold polypectomy) were performed in our hospital between September 2002 and December 2014. We retrospectively assessed these cases with respect to the following factors: patient factors which comprised age, sex, use of antithrombotics, type of antithrombotics (anticoagulant, aspirin, thienopyridine, and other antiplatelets), use of heparin bridge (HB), and total number of polyps in one examination; and lesion factors which consisted of location, gross type, size, resection method, and pathology. Antithrombotics were generally discontinued a minimum days before polypectomy. PPB was considered as hematochezia requiring emergency endoscopic hemostasis within 30 days after a polypectomy. The chi-square test was used to compare PPB rates between the groups with antithrombotics and the group without antithrombotics. The chi-squared test, Wilcoxon rank sum test, and multivariate logistic regression were used to assess factors associated with PPB (significance: $p < .01$). Statistical analysis was performed using Stata SE version 10.1.
**Results:** Among the patients who received anticoagulants, the PPB rate for HB use and nonuse was 28.6% (4/14) and 3.2% (4/127), respectively ($p < .001$). Among the patients who received anticoagulants but did not receive HB, the PPB rate for each antithrombotic was as follows: anticoagulant only, 2.3% (2/87, $p = .076$); anticoagulant + aspirin, 3.9% (1/26, $p = .054$); anticoagulant + aspirin + thienopyridine, 16.7% (1/6, $p < .001$); anticoagulant + aspirin + other antiplatelets, 0% (0/3, $p = .885$); and anticoagulant + other antiplatelets, 0% (0/5, $p = .852$). Among the patients who did not receive anticoagulants, the PPB rate for each antithrombotic was as follows: aspirin only, 0.6% (2/335, $p = .846$); thienopyridine only, 0.8% (1/121, $p = .855$); other antiplatelets only, 0% (0/244, $p = .194$); aspirin + thienopyridine, 3.9% (3/77, $p = .001$); and aspirin + other antiplatelets, 0% (0/60, $p = .519$). A multiple regression analysis of the cases that did not receive HB identified that the following patient factors: age (OR 0.95 [95%CI 0.93–0.97], $p < .001$), total lesion number per procedure (OR 1.31 [1.20–1.43], $p < .001$), and anticoagulant + antiplatelets (OR 7.94 [1.77–35.7], $p = .007$), were independent risk factors for PPB, whereas the following lesion factors: size (OR 3.05 [1.66–5.61], $p < .001$) and anticoagulant + antiplatelets (OR 9.34 [3.22–27.1], $p < .001$), were independent risk factors for PPB.
**Conclusion:** Based on our results, HB was a major risk factor for PPB. Meanwhile, of those who did not receive HB, anticoagulant + antiplatelets was a significant risk factor for PPB even after its use had ceased.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0345 SENTIFIT 270 SYSTEM CLINICAL PERFORMANCE EVALUATION COMPARED WITH OC SENSOR DIANA, FOR THE DETECTION OF HUMAN HAEMOGLOBIN AS FAECAL OCCULT BLOOD (FOB)

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**Introduction:** The SENTiFIT system (SENTiFIT assay) composed of the SENTiFIT 270 Analyser, the FOBGold reagents and the SENTiFIT pierceTube, is a specific system for the detection of human haemoglobin present in faeces, known as the FOB (faecal occult blood) test. The SENTiFIT assay is a quantitative FIT test (Faecal Immunochemical Test), highly recommended for both routine diagnostic testing and the CRC (ColoRectal Cancer) screening program. Faecal samples are collected and stabilized using the SENTiFIT pierceTube, whereas, the FOBGold latex reagent is optimized for the agglutination reaction with haemoglobin, analysed on the SENTiFIT 270 Analyser, a bench-top fully automated clinical chemistry instrument.
**Aims & Methods:** The aim of our study was to evaluate the clinical performances of the SENTiFIT FOBGold latex test using the SENTiFIT 270 system, and comparing it with the OC SENSOR DIANA system (DIANA assay), both FIT quantitative assays. Patients and Methods: Overall, 134 patients were enrolled in our prospective pilot clinical study. Patients were undergoing routine outpatient diagnostic workup and subsequent monitoring for the detection of Human Haemoglobin in the faeces. Two sets of 3 collection tubes (numbered 1 to 3), each for both assays (SENTiFIT assay and DIANA assay) were given to all patients along with detailed instructions on how to collect faecal samples. The patients were asked to collect 3 different bowel movements, using both collection tubes. A clinical provider emphasized the importance of collecting a sample from different areas of the faeces with both sticks and then after, rolling the tube sticks against each other for fecal homogenization. The initial approach for results

analyzing, for both assay, was using a cut-off level of 100 ng/mL for "positive" results.
**Results:** A total of 387 collection tubes of the DIANA assay and 387 collection tubes of the SENTiFIT assay were considered adequate for our study. The SENTiFIT assay identified 52 samples as positive (of these, the DIANA assay identified 28 samples), and 335 samples as negative (all but one were identified as negative by the DIANA assay). 25 samples were found discrepant, corresponding to 6.4% of total samples. Considering 100 ng/mL as threshold level, the total concordance percentage was 93.5%, and the AUC (Area Under the Curve) was 0.95.
**Conclusion:** Herein we report the results of a unique clinical comparison evaluation study of the SENTiFIT assay using the SENTiFIT 270 automated system. For the first time, we conducted a clinical study on a large scale of patients undergoing routine diagnostic FIT testing, using 2 different collection tubes for each of the 3 bowel movements. Our data show a significant correlation between the SENTiFIT assay and the DIANA assay, with a sensitivity of 96.6% and specificity of 93.3%. Although significant importance was given to sample collection and fecal homogenization instructions, we could assume that the possible reasons for discrepant results, as already shown by others, were due to sample collection (sampling by patient at home) and feces variability and stability. Applying higher cut-off levels (>100 ng/mL) on the SENTiFIT assay showed fewer discrepant results. According to the above, we could consider the SENTiFIT 270 system as a potential clinical assay for faecal immunochemical test.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0346 CORRELATION BETWEEN THE NATURE OF POSTPOLYPECTOMY BLOODY STOOL AND THE RISK OF POSTPOLYPECTOMY BLEEDING

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**Introduction:** Postpolypectomy bleeding (PPB) is a significant adverse event related to colonic polypectomy. However, little is known about the correlation between the nature of bloody stool within 24 hours after polypectomy and the risk of PPB. We aimed to evaluate the correlation between the nature of the bloody stools and PPB, using the photo-documented bloody stool data of the patients during immediate postpolypectomy period (<24 hours after polypectomy).
**Aims & Methods:** Between October 2015 and March 2016, 2, 514 patients underwent colonoscopic polypectomy in Asan Medical Center. In-hospital post procedural monitoring was provided for 927 of them at the specialized, short-term care unit for therapeutic colonoscopic procedures. During the in-hospital post procedural monitoring, the nurses routinely check the nature of the patients' first stools after polypectomy and take a snapshot of the stool in the toilet bowel, if it contains any bloody components. Forty-two of 927 patients (4.5%) reported that hematochezia or blood in stool. The photos were scored from 1 to 4 by three experienced endoscopists as follows: only a streak of blood or few blood clots (score 1), a handful of blood clots in the background of normal stool-colored fluid (score 2), pinkish, bloody fluid with or without clots (score 3), and moderate to large amount of fresh blood (score 4). The scoring endoscopists were blinded from the score data of other endoscopists and the patients' clinical outcomes. The score concordant in 2 or more endoscopists were confirmed as the final score for the photo (postpolypectomy bloody stool score, PBSS). Based on these scores, patients were divided into two groups based on the: high PBSS (score 3, 4) and low PBSS (score 1, 2) groups.
**Results:** Of 42 patients, 6 (14.3%), 22 (52.4%), 9 (21.4%), and 5 (11.9%) patients were scored 1, 2, 3, and 4, respectively. The PBSS scores were positively correlated with clinically significant PPB (spearman's $\rho = 0.526$). Based on the PBSS, 14 patients were categorized into the high PBSS group and 28 were into the low PBSS group. Second-look colonoscopy was performed for 5 (17.9%) of the low PBSS group and 10 (71.4%) of the high PBSS group ($P = 0.001$). Endoscopic hemostasis was required in 3 (10.7%) of the low PBSS patients and 8 (57.1%) of the high PBSS patients ($P = 0.001$). There were no significant differences in characteristics of patients and colon lesions between 2 groups. Among all the patients discharged without any treatment ($n = 27$), 2 patients in low PBSS group and 1 patient in high PBSS group developed delayed PPB. One of the 3 patients was large polyp (>20 mm) with long stalk, and the other 2 patient had multiple polyps more than 5.
**Conclusion:** The nature of bloody stool immediately after polypectomy is associated with the significant bleeding stigmata at the second-look colonoscopy and the risk of clinically significant PPB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0347 ADENOMA RECURRENCE RATES AFTER CURATIVE RESECTION FOR RIGHT-SIDE OR LEFT-SIDE COLONIC CANCER

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**Introduction:** Patients with history of colorectal cancer (CRC) are at increased risk of developing metachronous lesions including adenoma and cancer. We aim to determine the rates of colorectal polyp and adenoma recurrence on surveillance colonoscopy in patients after colonic resection for right-side (R-CRC) and left-side CRC (L-CRC).
**Aims & Methods:** Consecutive patients with CRC who had undergone surgical resection in our hospital between January 2001 and December 2003 were identified from our colorectal cancer database. Patients were included only if they had undergone surgical resection for curative intent and had a clearing colonoscopy performed either before or within 6 months after the operation. Patients with familial colorectal cancer syndrome (familial adenomatous polyposis, hereditary non-polyposis colorectal cancer syndrome), subtotal or total colectomy, and inflammatory bowel syndrome were excluded. Findings of surveillance colonoscopy performed up to 5 years after colonic resection were included in the analysis. Patient's baseline characteristics, tumor locations, type of surgical intervention and surveillance colonoscopy findings were retrieved. R-CRC was defined as cancer at and proximal to splenic flexure and L-CRC included all other distal cancers.
**Results:** 857 patients underwent surgical resection for CRC during the study period and 430 patients (146 patients with R-CRC and 284 with L-CRC) fulfilled our inclusion criteria. Among them, 88 (60.3%) patients with R-CRC and 204 (71.8%) patients with L-CRC had at least one surveillance colonoscopy, with a total of 447 colonoscopies performed. The rates of metachronous lesions found on surveillance colonoscopy were shown in the Table. The proportion of patients who had polyp and adenoma detected on surveillance colonoscopy was higher for those who had surgery for L-CRC compared to those who had surgery for R-CRC. There was also a significant difference on the time to polyps and adenoma recurrence between the two group, with a higher rate in the L-CRC group (log rank: $p = 0.04$ and 0.03 respectively). However, there was no significant difference on the detection of serrated lesions.

Detection Rates of Adenoma and Polyp on Surveillance Colonoscopy

| | R-CRC | L-CRC | P |
|---|---|---|---|
| Any polyps | 22.7% | 35.3% | 0.04 |
| Any adenoma | 14.5% | 26.5% | 0.03 |
| Advanced adenom | 5.7% | 8.3% | 0.63 |
| Cancer | 2.3% | 0.5% | 0.90 |
| Serrated lesions | 8.0% | 8.3% | 1.0 |

**Conclusion:** Patients who had surgery for L-CRC have a higher chance of developing metachronous polyps and adenoma than those with R-CRC. Our findings may call for a different surveillance strategy for patients with L-CRC or R-CRC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0348 HOW SIGNIFICANT IS THE ASSOCIATION BETWEEN METABOLIC SYNDROME AND PREVALENCE OF COLORECTAL NEOPLASIA?

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**Introduction:** The incidence and prevalence of metabolic syndrome (MS) and colorectal cancer (CRC) has been rising in developed countries. The association between these two diseases has been widely studied and published. Less evidence is available about the relation between MS and CRC precancerous lesions (adenomatous polyps, adenomas).
**Aims & Methods:** To assess the prevalence of colorectal neoplasia (adenomas, advanced adenomas) in individuals with high metabolic risk factors – type 2 diabetes mellitus (DM2) and cardiovascular risk (SCORE > 10%). Evaluate the outcomes in the CRC screening. Prospective, multicenter study was performed from January 2013 to December 2015. 2, 000 individuals aged 45–75 years were enrolled; 1, 000 in the target group (metabolic risk) and 1, 000 in the control group. All patients meet the screening population criteria (asymptomatic, without family or personal history of colorectal neoplasia) and were examined by colonoscopy at eight centers.
**Results:** 2, 071 individuals were enrolled and the first statistical analysis of 1, 500 completed records was finished. 726 persons (494 men, 68%) were enrolled in the target group (high metabolic risk) and 774 persons (353 men, 46%) in the control

group (without metabolic risk). The significantly higher prevalence of advanced adenomas was observed in the target group (18%; 95% CI 15–21%) comparing to the control group (9%; 95% CI 7–11%); OR 1.8; p = 0.002. Similarly, the prevalence of all adenomas was higher in the target group (48%; 95% CI 44–51%) than in the control group (35%, 95% CI 32–38%); OR 1.2, however the difference was not statistically significant (p = 0.179). Individuals with isolated high cardiovascular risk had higher prevalence of both, non-advanced adenomas (51%, 95% CI 46–56%; p = 0.327) and advanced adenomas (22%, 95% CI 18–26%; p = 0.049) comparing to the individuals with isolated DM2. Advanced adenomas were more likely in patients aged 65 – 75 years.

**Conclusion:** Individuals with a higher metabolic risk (cardiovascular; DM2) have two times higher risk of advanced adenomatous polyps. The individualized colorectal cancer screening should be considered namely in the individuals aged 65 – 75 years with SCORE > 10%. This project has been supported by the Czech Ministry of Health grant NT 13673.

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## P0349 ADHERENCE TO COLORECTAL CANCER SCREENING: 4 ROUNDS OF FECAL IMMUNOCHEMICAL TEST BASED SCREENING

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**Introduction:** The effectiveness of fecal immunochemical test (FIT) based screening programs is highly dependent on consistent participation over multiple rounds. Data on participation rates and characteristics of persons participating and not participating in repeated screening rounds are scarce.

**Aims & Methods:** We evaluated adherence to FIT-screening over 4 rounds and aimed to identify determinants for participation behavior. A total of 23, 339 randomly selected asymptomatic individuals aged 50–74 years were invited for biennial FIT screening from 2006 through 2014. All selected individuals were eligible and invited for every consecutive round, except for those who had moved out of the area, passed the upper age limit, or had tested positive in a previous screening round. One reminder letter was sent to non-responders after 6 weeks. For analyses of adherence, only invitees who were eligible at least for two rounds were included. Data on age, sex and socioeconomic status (SES) were recorded. Outcomes included participation rate per round, response to a reminder letter and behavioral differences in adherence to screening grouped by age, sex and SES.

**Results:** During the 4 rounds, overall participation rates remained stable at 60.4% (95% CI 59.6–61.2), 59.5% (95% CI 58.7–60.3), 61.8% (95%CI 61–62.6) and 62.5% (95% CI 61.8–63.5) respectively, with significantly higher participation rates for women across all 4 rounds (p < 0.001). Overall, 71.9% of the invitees attended at least once (12, 455 of 17, 312 invitees) and 28.1% never participated (4, 857 of 17, 312 invitees). The proportion of consistent participation (i.e. attending all rounds when eligible) was 47.8% (8, 271 of 17, 312 invitees). Consistent participation was associated with older age, female gender and a higher SES (Table 1). Offering a reminder letter in the first round increased uptake with 11.8%, during following screening rounds this resulted in an additional uptake of up to 10%.

**Table 1:** Predictors of adherence to FIT screening per category of participation behavior.

| | Consistent (n = 8271, 47.8%) | Inconsistent (n = 4184, 24.2%) | Never (n = 4857, 28.1%) | p-value |
|---|---|---|---|---|
| Age (median; (IQR)) | 57 (52-63) | 55 (51-61) | 55 (51-62) | p < 0.001 |
| Sex (male, %) | 45.4 | 50 | 54.1 | p < 0.001 |
| SES (%) -Low -Average -High | 7.4 70.5 22.1 | 10.7 72.2 17.1 | 13.9 70.4 15.7 | p < 0.001 |

**Conclusion:** In this population-based biennial FIT-screening cohort, participation over consecutive rounds was high and remained stable. Still, the substantial proportion of inconsistent participants suggest the existence of incidental barriers to participation, that, if possible, should be identified and removed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0350 AGING, CURRENT SMOKING AND METABOLIC FACTORS ARE INDEPENDENTLY ASSOCIATED WITH THE PREVALENCE OF COLORECTAL NEOPLASIA IN JAPAN: ANALYSES OF COMPREHENSIVE HEALTH CHECKUP DATA

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**Introduction:** Colorectal cancer (CRC) is the third leading cause of cancer death in Japan. For the past decades, the incidence and mortality rate of CRC has been increased in Japan which corresponds with the 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 & Methods:** In the present study, we investigated the risk factors such as metabolic and lifestyle factors for the occurrence of colorectal neoplasia (CRN) including adenomatous polyps as precancerous lesionsby using comprehensive health checkup data. We conducted a retrospective analysis in clinical practice at a single center. Among 7213 subjects who took comprehensive health checkup at our hospital between in August 2012 and July 2015, 1835 subjects who also underwent screening colonoscopy were enrolled. Sixty-three subjects were excluded for analyzes because they did not take computed tomography (CT) for visceral fat area (VFA) measurement. In the present study, CRN was defined as adenomatous polyp ≥ 5 mm in size and adenocarcinoma. A diagnosis of MetS was made by Metabolic Syndrome Diagnostic Criteria Exploratory Committee in Japan. Demographic characteristics, anthropometric measurements, 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 was evaluated by univariate analysis using t-test, $\chi 2$ 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 1772 subjects (men: 1206, women: 566) analyzed, 195 subjects had CRN (11.0%) and 5 had invasive colorectal cancer (0.3%). Four hundred and forty-six subjects were diagnosed as MetS (25.2%; 31.3% in men, 12.0% in women) and presence of MetS was significantly associated with CRN both in men (p = 0.016) and women (p < 0.01). Univariate analysis identified significant association of age, body mass index (BMI), VFA, systolic blood pressure (SBP), low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides (TG), fasting plasma glucose, hemoglobin A1c (HbA1c), fatty liver, current smoking habits, current drinking habits and ≥10 kg weight gain compared with the body weight at the age of twenty with prevalence of CRN. Logistic regression analysis revealed that age, current smoking, BMI, SBP, LDL and HDL-cholesterol and TG were independent factors associated with CRN prevalence (Table).

Logistic regression analysis

| | OR | 95% CI | p value |
|---|---|---|---|
| Age per 1 year increment | 1.046 | 1.031–1.062 | 0.000 |
| current smoking vs non-smoker | 2.445 | 1.617–3.697 | 0.000 |
| BMI per 1 kg/m$^2$ increment | 1.068 | 1.019–1.119 | 0.006 |
| systolic blood pressure per 1 mmHg increment | 1.013 | 1.004–1.021 | 0.004 |
| LDL-cholesterol per 1 mg/dL increment | 1.009 | 1.003–1.014 | 0.001 |
| HDL-cholesterol per 1 mg/dL increment | 1.013 | 1.001–1.026 | 0.035 |
| triglyceride per 1 mg/dL increment | 1.002 | 1.000–1.003 | 0.011 |

**Conclusion:** The present study demonstrated that metabolic factors in addition to aging and current smoking might be risk factors for CRN in Japan. This may help to identify high-risk subjects in CRC screening strategies.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0351 SECOND REORGANISED CYCLE OF NATIONAL COLORECTAL CANCER SCREENING PROGRAMME IN CROATIA

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**Introduction:** Colorectal cancer (CRC) was the second leading cause of cancer mortality in both men and women in 2013. in Croatia, (1.182 males and 855 females). Incidence is also on a second place among malignant neoplasms with 3.070 cases in 2013. with crude rate 71.6/100.000 (1.837 males and 1.233 females). The National Colorectal Cancer (CRC) Screening Program was established by the Ministry of Health, and started at the beginning of 2008. The second cycle lasted from October 2013. to April 2016. and it was performed in reorganised form.

**Aims & Methods:** Invitations included average population born between 1939 and 1963. The fecal occult blood test (FOBT) was performed by guaiac Hemognost card-test (Biognost). Each participant was invited to respond to invitation letter, and test cards with return envelope were mailed to responders. They had to fill the questionnaire and to send it together with the stool specimen of three consecutive bowel movements on test cards to the county public health institute for further reading. Person was considered as positive if 1 or more out 12 windows were positive. All positive persons were invited to colonoscopy within 6 weeks, and their GP was informed about that finding. A descriptive analysis of results was performed.

**Results:** A total of 1,331,910 individuals (100% of eligible from population database) were invited to screening by the end of 2016. In total, 353,164 (26.5%) persons returned the envelope with a completed questionnaire, while 81,837 were in one of groups with reason for nontesting. According to preliminary results, 184,084 persons returned test cards with a correctly applied stool specimen on FOBT cards. Until now, 7,630 (4.1%) FOBT positive patients have been found. Colonoscopy was performed in 6,120 patients (80%), and identified colorectal cancers in 205 patients (3.3% of colonoscopied, 2.6% of FOBT-positive, and 0.11% of all screened individuals). Polyps were found and removed in 1,328 (22% of colonoscopied) patients.

**Conclusion:** Second cycle implementation characteristics are: better compliance to screening invitation, especially in some counties, but still relatively low FOBT compliance; lower number of FOBT-positive persons than in first cycle, consecutively lower number of pathologic findings (polyps and cancers). Among organisational problems we detected problems with population database, lack of gastroenterology units, connection to informatised web-based screeening registry which is connected with GPs' application. Due to that, there is possible underregistration of examined participants. These results suggest a need for continous educational activities to improve awareness of CRC screening usefulness among target population as well as included health workers. Another problem is lack of colonoscopy equipement and in few counties lack of personnel. Continous improvement of CRC screening programe is needed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0352 EARLY PERFORMANCE INDICATORS OF THE COLORECTAL CANCER SCREENING PROGRAMME IN NAVARRA (SPAIN): HIGH PARTICIPATION AND ACCEPTANCE RATE

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**Introduction:** In Navarra colorectal cancer (CRC) represents the highest incidence of cancer, the second cause of cancer mortality in men and the first in women. This implies an important public health problem, which justifies the development of control strategies. Moreover, various studies demonstrate that CRC screening programmes are cost-effective, and a determining factor for the successful of them is the participation rate and the adherence.

**Aims & Methods:** The aim of this study was to assess the global participation, from the invitation until the confirmatory diagnostic procedure during the first fifteen months of the colorectal cancer screening programme in Navarra, started in 2013 and based on a quantitative immunochemical fecal occult blood (i-FOBT). The following indicators were analyzed:.

**1. Target population:** people born between 1.1.1944 and 31.12.1964, who reside in Navarra.

**2. Exclusion criteria:** colonoscopy performed in the previous 5 years, previous diagnosis of CRC, follow-up colonoscopies because of colon disease and severe illness that involves a contraindication for the participation.

**3. Invited population:** people who have received an invitation to participate in the CRC screening programme during the first fifteen months.

**4. Acceptance:** expression of their willingness to participate.

**5. Participation:** number of people who provide their i-FOBT sample. The reasons for non-participation were collected through randomized telephone interviews (n = 250).

**6. Rate of referral for follow-up confirmatory diagnostic procedure** (colonoscopy or virtual colonoscopy**) after a positive i-FOBT.**.

**Results:** Firstly, 10, 664 people were excluded following the criteria described above from our target population (160, 000). Invited population during the first fifteen months was composed of 46, 189 people. However, 31, 107 expressed their willingness to participate and 26.752 (65.29%) provided their i-FOBT (66.97% for women and 63.41% for invited men). The most frequent reasons for non-participation were laziness and lack of time (30%), and also lack of risk of disease perception (26%). In total, 1914 people had a positive i-FOBT and 36 (1.9%) of them refused to continue with the confirmatory diagnostic procedure. In this period, 1145 people had followed-up confirmatory diagnostic procedure, 1244 colonoscopies and 25 virtual colonoscopies were performed.

**Conclusion:** We have obtained a high rate of acceptance and participation in the colorectal cancer screening programme in Navarra with a participation rate (PR) of 65.29% and also an acceptance rate of follow-up confirmatory diagnostic procedure of 98.1%. Both values exceed quality indicators and recommended standards of the European guidelines. (1) It is important to highlight that our programme participation rate is one of the highest in Spain (PR: 21% - 64.3%) and in Europe (7 – 67.7%), with similar rates to the Basque Country (PR: 64.3%) and Finland (PR: 67.7%) programmes. (2) To conclude, further studies are required for assessing the factors that have most significant influence in the PR of the CRC screening programmes. Nevertheless, the important lack of risk of disease perception in the non-participation group from our target population is an issue to be analyzed and addressed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0353 DEVELOPMENT OF COLITIS-ASSOCIATED COLORECTAL CANCER DEPENDS ON THE ACTIVITY OF THE ENDOGENOUS OPIOID SYSTEM

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**Introduction:** Morphine is still a gold standard in the treatment of patients with malignant tumors and those suffering from severe cancer pain. Its potent antinociceptive activity improves quality of life and is an advantage over side effects caused by chronic administration. Recent studies revealed that stimulation of opioid receptors produces different effects on cancer progression depending on the cancer type, stage of disease, etc. Therefore, before deciding on the type of therapy, in order to predict the course of, and estimate the patient's response to the intended treatment, it may be useful to consider possible involvement of genetic variability in opioid system activity. An animal model based on two mouse lines, displaying high (HA) and low (LA) activity of the endogenous opioid system has recently been employed for studies on the effects of opioids in the gastrointestinal (GI) tract. So far the usefulness of the HA/LA model has been validated for investigations on the GI motility.

**Aims & Methods:** The aim of our study was to characterize the role of the endogenous opioid system in the development of colitis-associated colorectal cancer in HA and LA mouse lines. Ten-week-old male Swiss-Webster mice bred using bidirectional selection and classified as HA or LA line based on the measurement of analgesia (hot plate and tail-flick tests) were used in this study. Colitis-associated colorectal cancer was induced by a single intraperitoneal injection of azoxymethane (10 mg/kg) and subsequent addition of dextran sodium sulfate (2% w/v) into drinking water (days: 7–14, 35–42, 63–70). The body weight and clinical score (rectal bleeding, stool consistency) were controlled. After 12 weeks, the macroscopic colon damage score was assessed and the samples for biochemical, molecular and histological studies were collected.

**Results:** A significant difference in tumor development between HA and LA lines in the mouse model of colitis-associated colorectal cancer was observed. In the HA mouse line, hyperactivity of the endogenous opioid system increased two-fold the number of tumors as compared to the LA mouse line. Myeloperoxidase activity, a measure of neutrophil infiltration, was also significantly increased in HA vs. LA mouse line. Moreover, LA mice were in good general health throughout the entire experimental period comparing to HA mouse line. Hematoxylin and eosin staining confirmed a significant difference between HA and LA mouse lines as indicated by histology score (muscle thickness, damage of the intestinal wall, immune cell infiltration, invasion depth, crypt hyperplasia and disruption).

**Conclusion:** Our data suggest that hyperactivity of the endogenous opioid system may be crucial in tumor development and progression in colitis-associated colorectal cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0354 PROMOTER HYPOMETHYLATION AND OVEREXPRESSION OF LINC00152 LONG NON-CODING RNA DURING DEVELOPMENT AND PROGRESSION OF COLORECTAL CANCER

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**Introduction:** Long non-coding RNAs (lncRNAs) contribute to the development of different cancers including colorectal cancer (CRC). LINC00152 lncRNA has an oncogenic function in gastric cancer cell lines. Expression and effects of LINC00152 during colorectal carcinogenesis and cancer progression are not well studied.
**Aims & Methods:** We aimed to analyze LINC00152 expression and promoter DNA methylation changes along the colorectal normal-adenoma-carcinoma sequence. Possible gene expression regulatory role of LINC00152 was also studied in connection with DNA methylation regulation and with microRNAs which can be targeted by LINC00152. 147 colonic biopsy samples (49 normal, 49 adenoma, 49 CRC) were analyzed using HGU133Plus2.0 microarrays (Affymetrix). Real-time PCR validation was performed on 90 colonic specimens. DNA methylation was studied in 30 colonic tissue samples (15 adenoma, 9 CRC, 6 normal) using methyl capture sequencing. Methylation status of LINC00152 promoter was validated on 90 biopsy samples by bisulfite sequencing. Parallel LINC00152, microRNA, mRNA expression analysis was carried out using Human Transcriptome Array 2.0 and miRNA 3.0 Array data of 24 colonic biopsies.
**Results:** LINC00152 (Affy ID: 225799_at) was found significantly upregulated in adenoma and CRC samples compared to normal tissue ($p < 0.001$) which was confirmed by real-time PCR. Remarkable hypomethylation of LINC00152 promoter region was detected in CRC compared to normal samples using both methyl capture sequencing and bisulfite sequencing ($p < 0.01$), which was correlated with increased LINC00152 expression ($R = 0.90$). In parallel with LINC00152 overexpression, downregulation of certain microRNAs potentially targeted by LINC00152 (including miR-195-5 p) was found in CRC, while certain validated targets (like CDK4, CCND1) of these microRNAs were significantly upregulated ($p < 0.01$). In silico analysis revealed potential interactions between LINC00152 and promoters of tumor suppressor genes such as p15 and p21.
**Conclusion:** Promoter hypomethylation and overexpression of LINC00152 lncRNA can contribute to colorectal carcinogenesis facilitating cell proliferation through downregulation of miRNAs targeting cell cycle progression genes or affecting promoter methylation of tumor suppressor genes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0355 CONTRIBUTION OF THE MEK5/ERK5 PATHWAY TO COLON CANCER STEM-LIKE CELL PROPERTIES

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**Introduction:** Cancer stem cells are currently viewed as the reservoir of cells responsible for tumour development, metastasis and drug resistance. However, the molecular players underlying cancer stem cell self-renewal and chemoresistance remain poorly understood. We have previously demonstrated that the MEK5/ERK5 signalling pathway promotes colon cancer metastasis, and that ERK5-targeted inhibition enhances the anticancer properties of 5-fluorouracil in a murine xenograft model.
**Aims & Methods:** In the present study, we aim to understand the contribution of MEK5/ERK5 signalling for the regulation of the balance between self-renewal and differentiation in colon cancer stem cells. The effect of MEK5/ERK5 signalling inhibition was investigated in human colon cancer stem-like cells using both genetic and pharmacological approaches. For this purpose, HCT116, HT29, SW480 and SW620 colon cancer cells were cultured for three generations in sphere-forming conditions. The number of tumour spheres and cells per sphere was determined for each generation. The levels of CD44/CD133 expression and aldehyde dehydrogenase 1 (ALDH1) activity were evaluated by flow cytometry. Additionally, the mRNA expression of established stemness markers was evaluated by SYBR Real-Time PCR.
**Results:** Our results demonstrate that tumour spheres enriched in colon cancer stem-like cells have significantly higher levels of MEK5 and ERK5 phosphorylation when compared with their adherent counterparts. In turn, ERK5 inhibition using the pharmacological inhibitor XMD8-92 decreased the number and size of spheres in HCT116, HT29, SW480 and SW620 cells over three generations ($p < 0.05$). Similarly, ERK5 inhibition using a dominant negative form of MEK5 decreased HCT116 sphere-forming ability, significantly reducing the number of cells per tumour sphere in third generation spheres, as compared to controls ($p < 0.01$). In addition, ERK5 pharmacological inhibition significantly reduced the proportion of CD44/CD133-positive cells ($p < 0.05$), as well as the percentage of cells with high ALDH1 activity. Finally, mRNA expression levels of stemness markers Sox2, Oct4, Lgr5 and Bmi1 were also negatively regulated by XMD8-92 in SW620 spheres ($p < 0.05$).
**Conclusion:** Our results indicate that MEK5/ERK5 pathway activation may contribute to sustained stemness in colon cancer cells, suggesting ERK5 inhibition as a potential therapeutic strategy to target colon cancer stem cells and improve colon cancer treatment. Supported by UID/DTP/04138/2013, SFRH/BD/96517/2013 and SFRH/BD/88619/2012 from FCT, Portugal.
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## P0356 SELECTIVE INHIBITION OF FATTY ACID AMIDE HYDROLASE INHIBITOR PF-3845 DECREASES VIABILITY, MIGRATION AND INVASIVENESS OF HUMAN COLON ADENOCARCINOMA COLO-205 CELL LINE

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**Introduction:** Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the third leading cause of cancer death worldwide. Thus, it is clear that there is an urgent need for developing effective anti-cancer agents and promising approaches that will improve clinical outcomes in CRC patients. Earlier reports suggest that cannabinoids may inhibit tumor growth both in vitro and in animal models. The aim of our study was to characterize the influence of selected inhibitors of the enzymes involved in the synthesis and degradation of endocannabinoids on colon cancer cell viability, invasiveness and migration.
**Aims & Methods:** The human colon adenocarcinoma Colo-205 cells were incubated with PF-3845, JZL-184 and RHC-80267 (inhibitors for fatty acid amide hydrolase (FAAH), mono- (MAGL) and diacylglycerol lipase (DAGL), respectively) for 48 h. To determine cell viability, the colorimetric MTT metabolic activity assay was used. Next, Colo-205 cells were incubated with PF-3845 alone or with PF-3845 together with selected antagonists: AM 251, AM 630, SB 366791, RN 1734 and G-15 ($CB_1$, $CB_2$, TRPV1, TRPV4 and GPR30 antagonists, respectively). Furthermore, we characterized the expression of $CB_1$ and $CB_2$ receptors by Western blot analysis and assessed the effect of PF-3845 on Colo-205 cell migration and invasiveness.
**Results:** We observed that PF-3845 was the most efficient in decreasing Colo-205 cell viability ($IC_{50} = 52.55 \pm 4.75\,\mu M$). Interestingly, this effect was enhanced when Colo-205 cells were incubated with PF-3845 and RN-1734, a TRPV4 antagonist ($IC_{50} = 30.54 \pm 5.36\,\mu M$). Furthermore, we noted a significant decrease ($p < 0.05$) in the expression of $CB_1$ receptor and a significant increase ($p < 0.001$) in $CB_2$ expression levels in response to treatment with PF-3845 compared with untreated control. We also demonstrated that PF-3845 at the concentrations of 25 $\mu$M and 50 $\mu$M significantly ($p < 0.001$) reduced migration and invasiveness of Colo-205 cells (by 49.57 and 71.28% versus control, respectively).
**Conclusion:** For the first time, we report that PF-2845 may play a crucial role in inhibiting viability, migration and invasiveness of Colo-205 cell line. Thus, our studies strongly support the hypothesis that modulation of the endocannabinoid turnover through inhibition of their hydrolysis could be a potential anti-cancer strategy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0357 SECRETION PROTEIN VSTM2A IS A NOVEL TUMOR SUPPRESSOR AND ASSOCIATES WITH COLORECTAL CANCER PATIENT SURVIVAL

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**Introduction:** Using genome-wide promoter CpG island screening and RNA-sequencing data, we have recently identified that V-set and transmembrane domain containing 2 A (VSTM2A) gene, which encodes a 26 kDa protein, was hypermethylated and silenced in colorectal cancer (CRC). However the role of VSTM2A in tumorigenesis has not been evaluated yet.
**Aims & Methods:** VSTM2A methylation status was evaluated by bisulfite genomic sequencing. The biological functions of VSTM2A were investigated in vitro

and in vivo. VSTM2A downstream effectors were elucidated by luciferase assay, real-time PCR and Western blot. The clinical impact of VSTM2A was assessed in 263 CRC patients.
**Results:** Full or partial methylation of VSTM2A promoter was found in CRC cell lines and tumor specimens, whilst none or low methylation was detected in the normal colon tissue specimens. Demethylation by 5-aza-2'-deoxycytidine restored VSTM2A expression in silenced CRC cell lines, indicating that promoter methylation contributed to the decrease expression of VSTM2A. VSTM2A mRNA was significantly reduced in all 8 CRC cell lines and in CRC cancer tissues compared with adjacent normal tissues ($n = 86$, $P < 0.05$). In keeping with this, VSTM2A protein expression was reduced in CRC tumors compared to their adjacent normal tissues detected by Western blot ($P < 0.05$) and immunohistochemistry analysis ($P < 0.01$). We further evaluated the association between VSTM2A protein expression level and survival of CRC patients by tissue microarray. A survival analysis of 158 CRC patients indicated that high VSTM2A protein expression was significantly correlated with longer overall survival ($P < 0.05$) and disease-free survival ($P < 0.05$). Our functional studies supported a tumor suppressive role of VSTM2A in CRC. Ectopic VSTM2A expression significantly suppressed CRC cell viability ($P < 0.01$) and reduced colony formation ($P < 0.01$). VSTM2A caused G2 phase cell cycle arrest ($P < 0.001$) and induced apoptosis ($P < 0.01$), concomitant with enhanced cell cycle regulators p21 and p27, and pro-apoptotic factors of cleaved caspase 3, caspase 8 and PARP. Subcutaneous tumor xenografts of CRC cells (HCT116 and DLD1) with stable VSTM2A expression in nude mice exhibited significant reduced tumor growth compared with the control cells ($P < 0.01$). We further investigated the molecular mechanisms of VSTM2A in CRC. VSTM2A could be detected in the cell culture supernatant. Inhibition of the cell secretion by Brefeldin A, which prevents secretory protein transport from the endoplasmic reticulum to the Golgi apparatus, inhibited VSTM2A supernatant expression and induced cytosolic accumulation, suggesting a secretory property of VSTM2A. Our results further indicated that secreted VSTM2A could attach to cell plasma membrane evidenced by Immunofluorescence and immunoprecipitation assays, inferring that VSTM2A exerted its biological function in a paracrine manner. Using luciferase reporter screening of 9 signal transduction pathways, we found that VSTM2A significantly inhibited Wnt signaling TOP-Flash luciferase reporter activity ($P < 0.01$). Moreover, VSTM2A suppresses Wnt signaling through inducing $\beta$-catenin phosphorylation and inhibiting Wnt downstream targets c-myc and cyclin D1 expression.
**Conclusion:** Secretory protein VSTM2A is a critical tumor suppressor in colorectal carcinogenesis through inhibiting Wnt signaling by suppressing $\beta$-catenin activation. High VSTM2A protein level was significantly correlated with better CRC patient outcomes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0358 MDM2 T309G POLYMORPHISM AND RISK OF COLORECTAL CANCER

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**Introduction:** Murine double minute 2 (MDM2) is an E3 ubiquitin-protein ligase that mediates cell cycle arrest by negatively regulating the tumour suppressor gene p53. Polymorphisms have been thought to be associated with colorectal cancer (CRC), however results have been largely inconclusive. A meta-analysis of MDM2 T309G (rs2279744) was conducted to clarify and assess whether any association could be found.
**Aims & Methods: Aim:** To perform a systematic review and meta-analysis to assess the association of MDM2 T309G polymorphism with the risk of CRC.
**Methods:** A systematic literature review of the Pubmed and HuGENet databases was conducted and studies were included/excluded based on pre-specified criteria. The per allele model was used to assess risk by calculating pooled odds ratios with 95% confidence intervals. Publication bias was investigated using a funnel plot. Statistical analysis was conducted using the R program (version 3.2.4).
**Results:** A total of 135 studies were screened and 6 case control studies were included with 3553 cases and 5781 controls. No association was found between MDM2 T309G and CRC ($OR = 1.25$; 95% CI 0.97–1.62). The funnel plot showed that publication bias was present.
**Conclusion:** This meta-analysis suggests that MDM2 T309G polymorphism is not associated with risk of CRC and should not be evaluated as part of a patient risk assessment. Future studies with larger and more varied ethnicities would allow more accurate assessment of the association between MDM2 T390G and CRC risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0359 UNTANGLING MOLECULAR ORIGINS OF COLORECTAL CARCINOMAS AND ASSIGNMENT OF MAJOR PATHWAYS BASED ON CIMP/MSI/BRAF/KRAS/TP53/APC PROFILES FROM ENDOSCOPIC TISSUE SAMPLING

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**Introduction:** Recent advances in molecular profiling have resulted in definition of molecular types of colorectal cancer based on genetic and epigenetic aberrations. Resulting from separate developmental pathways the different types are associated with distinct prognostic features, which can be utilized in clinical practice.
**Aims & Methods:** The aim of this study was to assign molecular subtypes based on CIN/CIMP/MSI molecular phenotypes in combination with mutation status of (proto) oncogenes KRAS and BRAF and tumor suppressors TP53 and APC in large adenomas and in early and late carcinomas for assessment of patients prognosis. A prospective 3-year study has resulted in the acquisition of samples (fresh biopsies or FFPE sections from EPE or EMR) from 138 carcinomas along with associated clinical parameters including localization, grade and histological type from adenomas and localization and stage for carcinomas. A complex molecular phenotyping has been performed on endoscopic tissue specimens using methylation-specific multiplex ligation-dependent probe amplification technique (MS-MLPA) for the evaluation of CpG-island methylator phenotype (CIMP), PCR fragment analysis for detection of microsatellite instability (MSI) and high-sensitive CE melting assay for multiplex detection of somatic mutations in KRAS, BRAF, TP53 and APC genes.
**Results:** We have identified carcinomas belonging into 5 major molecular subtypes: (i) 3x serrated CIMP+/BRAF+/MSI-; (ii) 9x serrated CIMP+/BRAF+/MSI+; (iii) 2x familial CIMP+/MSI+/BRAF-, (iv) 38x Traditional CIMP-/KRAS+/APC+ and (v) 18x Traditional CIMP+/TP53+. The remaining 68 carcinomas were resulting from other combinations.
**Conclusion:** The complex molecular profiling using combination of phenotypes with somatic mutations of oncogenes and tumor supressors allows for efficient stratification of carcinomas with subsequent assignment of prognosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0360 HIGH RATES OF DISCORDANCE BETWEEN BRAF AND MLH1 METHYLATION TESTS IN CRC PATIENTS OVER 70 YEARS OLD IN A LYNCH SYNDROME UNIVERSAL SCREENING PROGRAM

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**Introduction:** Universal screening of all colon cancers for Lynch syndrome (LS) through immunohistochemistry for DNA mismatch repair proteins is currently recommended. However, there are many false positive results due to somatic methylation of MLH1. Directly analyzing the MLH1 gene for promoter methylation is ideal but is costly and not widely available. BRAF mutation status has been proposed as a surrogate marker, but the performance of BRAF testing in the setting of a large screening population has not been defined.
**Aims & Methods:** To define the correlation between BRAF mutation status and MLH1 promoter methylation in a screening program for LS. To define the correlation between BRAF mutation status and MLH1 promoter methylation in a screening program for LS. A universal screening program for LS was established in 2 medical centers. Tumors with abnormal MLH1 staining had both BRAF and MLH1 promoter methylation analysis performed. Tumors positive for both were considered to be sporadic cancers. Formal genetic testing was recommended for all other cases.
**Results:** 1011 CRC cases were screened for LS over a 4-year period, and 148 (15%) exhibited abnormal MLH1 staining. Both BRAF and MLH1 hypermethylation testing was completed in 126 of these cases. Concordant results (positive for both BRAF mutation and MLH1 hypermethylation, or negative for both) were obtained in 86 (68%) and 16 (13%) cases, respectively. The overall concordance rate between MLH1 methylation and BRAF mutation status was 81%. The PPV and NPV for a BRAF mutation in predicting MLH1 promoter methylation were 99% and 41%, respectively. In patients 70 years or older, the NPV fell to 15% (vs. NPV = 68% in patients < 70 years). This decline in NPV was observed in both male and female patients, though it was much more pronounced in females (NPV = 6% in females ≥ age 70). If BRAF mutation testing had been used as a sole test to evaluate cases with abnormal MLH1 staining, there would have been a 2.3-fold increase in the number of referrals for genetic testing compared to the use of MLH1 methylation testing. However, a 2-tier approach in which BRAF is

performed on all cases and MLH1 methylation testing is then offered only for BRAF wild type (WT) cases would result in a comparable number of referrals for genetic testing when compared to MLH1 methylation testing in all cases. By reserving MLH1 methylation testing only for BRAF WT cases, there would be a decrease of almost 70% in the number of MLH1 methylation tests performed.
**Conclusion:** In a large prospective screening program for LS, BRAF mutation status has an excellent PPV but poor NPV in predicting MLH1 promoter methylation. This low NPV is attributable to a large number of BRAF WT/MLH1 methylation-positive cases in patients ≥ 70 years old. A tiered approach in which BRAF testing is performed in all cases and more costly MLH1 methylation is reserved for BRAF WT cases may reduce costs and facilitate wider implementation of LS screening programs.
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A.J. Iafrate: Dr. Iafrate has received royalties from ArcherDx.
All other authors have declared no conflicts of interest.

## P0361 IMPLEMENTATION OF A STRUCTURED E-LEARNING IMPROVES THE INTER-LABORATORY CONSISTENCY IN THE HISTOPATHOLOGICAL CLASSIFICATION OF SERRATED POLYPS

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**Introduction:** Sessile serrated lesions (SSL) are suggested to be the precursors of 15–30% of colorectal cancer (CRC). Distinguishing premalignant SSL from innocuous hyperplastic polyps (HP) tends to be difficult for pathologists in daily practice. As a result, the current European Society of Gastrointestinal Endoscopy surveillance guideline does not differentiate between histopathological subtypes of serrated polyps with regard to post-polypectomy surveillance advice, resulting in both over- as well as under-treatment.
**Aims & Methods:** We aimed to evaluate nationwide variability within histopathology laboratories in the frequency of diagnosing a SSL as compared to a HP within the Dutch Faecal Immunological Test (FIT)-based population screening program for colorectal cancer and to assess the potential beneficial effect of a structured e-learning on practice variation. Data of all resected serrated polyps within the national screening program were retrieved from the Dutch Pathology Registry (PALGA) from January 2014 to December 2015. An e-learning was developed, commissioned by the National Institute for Public Health and the Environment, and implemented among screening pathologists on October first 2014. Ratio between SSL and HP diagnosis was determined per laboratory. Mixed effects logistic regression was used to calculate adjusted odds ratios (OR) for the diagnosis of a SSL per laboratory, as compared to the median reference laboratory. To evaluate the effect of the e-learning on the variability within pathology laboratories, only those laboratories that assessed at least 50 lesions both before as well as after implementation of the e-learning were selected. Difference in practice variation before and after implementation was calculated using a Wilcoxon matched-pair signed-rank test.
**Results:** In total 14, 997 individuals with 27, 879 serrated polyps were included for analysis; 9, 244 (61.6%) were male and 8, 487 (56.6%) were above 65 years of age. Of all serrated polyps, 6, 665 (23.9%) were diagnosed as SSL and 21, 214 as HP (76.1%). Number of diagnosed serrated polyps ranged from 99 to 2238 (median 533) between 44 laboratories. The ratio of diagnosing a SSL as compared to all serrated polyps ranged from 5 to 47% (median 23%). In total 22 (50%) laboratories showed a significant different adjusted OR (range 3.47–0.16) for the diagnosis of an SSL as compared to the reference laboratory. Proportion of SSL diagnosis significantly increased after implementation of the e-learning (median 18 vs 25%; $P < 0.001$). After implementation, the adjusted OR of 23 out of 33 included laboratories shifted towards the reference, while 10 laboratories shifted away from the reference laboratory. Variability between laboratories significantly decreased after implementation ($p = 0.02$).
**Conclusion:** We demonstrated a substantial inter-laboratory variability in the histopathological classification of serrated polyps, which decreased after implementation of a structured e-learning. Results from this study might contribute to more homogeneous practice among pathologists in the diagnosis of SSL, by advocating awareness and training in an overarching and structured setting.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0362 THE GROWTH PATHWAY AND THE CLINICOPATHOLOGICAL CHARACTERISTICS OF DEPRESSED-TYPE COLORECTAL CARCINOMAS

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**Introduction:** Colorectal cancers are generally recognized to develop from protruded-type "polyps". This "adenoma-carcinoma sequence" theory has been in the mainstream of development of colorectal cancers. But 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.
**Aims & Methods:** The aim is to clarify the pathological features of depressed-type colorectal carcinomas compared with flat- and protruded -type. A total of 27599 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically in our Center from April 2001 to Dec 2015. Of these, 1097 lesions were T1 carcinomas. According to the morphological/development classification, 236 lesions (21.5%) were depressed-type, 373 lesions (34.0%) were flat-type and 426 lesions (44.4%) were protruded-type. We analyzed the pathological features of these lesions.
**Results:** The rate of submucosal invasion in all the lesions was 62.1% in depressed-type, 3.3% in flat-type and 2.8% in protruded-type. Within less than 5 mm in diameter, that was 10.6%, 0% and 0% respectively. Among T1 carcinomas, the rate of vessel invasion was 63.6% in depressed-type, 34.3% in flat-type and 38.7% in protruded-type, that of poorly differentiated or mucinous adenocarcinoma was 16.9%, 11.0% and 13.6%, that of massively submucosal invasion was 87.7%, 59.0% and 71.4%, and that of tumor budding was 36.9%, 16.4% and 17.3%, respectively. The rates of these pathological factors were significantly higher in the depressed-type lesions. On the other hand, the rate of adenomatous component was 5.1%, 52.5% and 50.8%, and the rate of polypoid growth was 16.1%, 53.1% and 95.3% respectively. It was significantly lower in depressed-type lesions, suggesting that they emerge directly from normal epithelium without going through the adenoma stage. The rate of lymph node metastasis was 10.2%, 3.2% and 9.1%, respectively. Among 1097 cases of T1 colorectal carcinomas, two cases showed synchronous metastasis and both were depressed-type lesions.
**Conclusion:** Depressed-type colorectal carcinomas invade massively even when they are small. They had higher risks of vascular invasion, poorly differentiated or mucinous adenocarcinoma, massive invasion, and tumor budding than flat- and protruded-types. For their rapid growth and malignant potential, whether the lesion is depressed-type or not is very important in the diagnosis of colorectal carcinomas.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0363 ELECTRONIC NOSE (AENOSE™) CAN DETECT COLORECTAL CARCINOMA IN EXHALED BREATH: A PILOT STUDY

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**Introduction:** With colorectal cancer (CRC) being the fourth leading cause of death of malignant diseases early detection in screening programs is essential. With a limited sensitivity for the most frequently used screening tool, the fecal immunochemical test (FIT), there is need for a better screening tool. We performed a first study to analyse volatile organic compound (VOC) patterns in exhaled air using an electronic nose.
**Aims & Methods:** In this proof of concept study we aimed to investigate with an electronic nose (Aenose™) whether patients with CRC have a specific VOC pattern compared to non-CRC patients. Breath samples of patients with a suspicion of CRC who were scheduled to undergo an elective colonoscopy were collected, as well as samples of patients with histologically proven CRC before undergoing surgery. The electronic nose (Aenose™) is equipped with three sensors. By using thermal cycling a four dimensional pattern (time, temperature, sensor response, sensor type) is obtained. These data were compressed using a Tucker3 algorithm, generating a 1-dimensional vector for each measurement. In this way, the electronic nose is "trained" to distinguish between healthy controls and patients with CRC. Sensitivity, specificity and the receiver operator characteristic (ROC) curves for detection of CRC were calculated.
**Results:** We obtained samples in 90 patients, mean age 65 years (range 40–85, 52% female). Of these 23 had CRC, and 67 served as controls. No differences in baseline characteristics were seen, besides a 3 years higher age in the CRC group. The colonoscopic findings in the control group encompassed normal findings ($n = 17$), hyperplasia ($n = 7$), adenomas with low ($n = 23$) and high grade dysplasia ($n = 1$), and colitis ($n = 5$). The VOC pattern from patients with CRC differed from the controls with a sensitivity of 96% and a specificity of 91%. The area under the ROC curve (AUC) was 0.93.
**Conclusion:** This study shows that patients with CRC and healthy controls have a different VOC pattern and suggests that this electronic nose is able to differentiate between these two. A validation study is needed for confirmation of these promising first results.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0364 CLINICOPATHOLOGICAL STUDY OF LATERALLY SPREADING TUMORS OF THE COLORECTUM

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**Introduction:** Laterally spreading tumors (LSTs) of the colorectum are classified into the following four subtypes according to their morphology; granular homogeneous type (LST-GH), granular nodular mixed type (LST-GM), non-granular flat-elevated type (LST-NGF), and non-granular pseudo-depressed type (LST-NGPD). Clinical features of each subtype of LSTs have not been fully evaluated.
**Aims & Methods:** The aims of this study was to clarify the clinicopathological features of colorectal LSTs focusing on their subtypes. We reviewed clinical

charts and surgical pathology files of 4402 endoscopically resected specimens during January 2007 and December 2015 at our institution. A total of 358 LSTs were detected. We examined the clinical features (mean age, male to female ratio, size, location, Incidence of concomitant carcinoma) according to their subtypes.
**Results:** Of these 358 lesions, a total of 117 (32.7%) were LST-GH, 29 (8.1%) LST-GM, 188 (52.5%) LST-NGF, and 24 (6.7%) LST-NGPD. Mean age of patients with each subtype was 68.7 years old for LST-GH, 66.1 for LST-GM, 68.6 for LST-NGF, and 67.9 for LST-NGPD. Male to female ratio (M/F) was 1.05 for LST-GH, 2.22 for LST-GM, 1.85 for LST-NGF, and 1.40 for LST-NGPD. Mean size of LST-GH (19.4 mm) and LST-GM (24.3 mm) were significantly larger than that of LST-NGF (15.1 mm) and LST-NGPD (13.9 mm). All subtypes were located predominantly in the proximal colon. Incidences of concomitant carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 22.2% (26 out of 117), 62.1% (18 out of 29), 16.0% (30 out of 188), and 71.4% (15 out of 21), respectively. Incidences of concomitant submucosal carcinomas in LST-GH, LST-GM, LST-NGF, and LST-NGPD were 0% (0 out of 117), 17.2% (5 out of 29), 1.1% (2 out of 188), and 25.0% (6 out of 24), respectively.
**Conclusion:** Each subtype of LSTs has distinct clinical features. LST-GM and LST-NGPD have higher malignant potentials than other subtypes. Especially LST-NGPD has the highest risk of invasive carcinoma regardless of its size. Therefore we should carefully detect these lesions and choose appropriate treatment according to the subtypes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0365 MICROVESSEL DENSITY OF NEOVASCULAR VESSELS COULD BE A PREDICTOR OF DISTANT METASTASIS OF COLORECTAL CANCER: IMMUNOHISTOCHEMICAL ASSESSMENT WITH CD105 ANTIBODY

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**Introduction:** It is thought that tumor growth is dependent on angiogenesis, which may also permit metastasis. CD105 (endoglin) is an accessory receptor of transforming growth factor (TGF)-$\beta$. It has been demonstrated that anti-CD105 antibody has high affinity for activated endothelial cells. Therefore, CD105 may be a specific marker for tumor angiogenesis. The relationship between neovascularization, assessed by CD105 antibody, and metastasis has been reported. However, it is still worthwhile to investigate the relationship between distant metastasis and CD105 antibody-positive microvascular density (MVD), along with potentially confounding clinicopathological factors.
**Aims & Methods:** We aimed to establish the relationship between CD105-antibody-positive microvessels and distant metastasis. We analyzed 126 colorectal adenocarcinomas that were endoscopically or surgically resected at Showa University Northern Yokohama Hospital between January and September 2009. We assessed microvessels by staining their endothelial cells with CD105 monoclonal antibody. We defined MVD as the number of microvessels per 400× field. MVD was counted by one pathologist (T.C.). In addition, clinicopathological factors were retrospectively analyzed and multivariate logistic regression was performed to predict the independent risk factors for distant metastasis.

**Table:** Multivariate logistic regression.

| Clinicopathological factors OR (95% CI) | | Multivariate analysis P value | |
|---|---|---|---|
| Age | (≥70/<70 years) | 1.24 (0.42–3.67) | 0.6962 |
| Sex | (male/female) | 1.34 (0.46–4.03) | 0.5947 |
| Tumor size | (≥30/<30 mm) | 1.15 (0.22–7.71) | 0.8736 |
| Location | (rectum/colon) | 1.20 (0.39–3.61) | 0.7488 |
| Tumor depth | (T2–T4/T1b) | 8.32 (0.76–238.54) | 0.1266 |
| Lymphatic invasion | (+/-) | 0.54 (0.12–2.21) | 0.3912 |
| Venous invasion | (+/-) | 3.88 (0.87-23.40) | 0.0983 |
| Regional lymph node metastasis | (+/-) | 6.22 (1.73–25.99) | 0.0074 |
| Por/Muc component | (+/-) | 0.65 (0.17–2.30) | 0.5182 |
| Adjuvant chemotherapy | (+/-) | 1.69 (0.47–6.13) | 0.4147 |
| MVD | (≥10/<10 per 400× field) | 3.84 (1.30–12.31) | 0.0176 |

CI, confidence interval; OR, odds ratio; Por/Muc, poorly differentiated adenocarcinoma / Mucinous adenocarcinoma.

**Results:** At the time of resection or during follow-up, 30 lesions had distant metastasis (liver, 12; lung, 4; peritoneum, 4; liver and peritoneum, 3; lung and peritoneum, 3; liver, lung and peritoneum, 1; liver and bone, 1; liver, lung, distant lymph node and bone, 1; lung, kidney and spleen, 1). The mean ± SD CD105-antibody-positive MVD in patients with distant metastases was significantly larger than in those without distant metastasis (10.5 ± 4.9 vs 7.6 ± 3.4; $P < 0.05$, Student's t test). Multivariate logistic regression indicated that CD105-antibody-positive MVD and regional lymph node metastasis were predictors of distant metastasis (Table).
**Conclusion:** Assessment of CD105-antibody-positive MVD could contribute to selecting patients who need more intensive surveillance after surgery for colorectal cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0366 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 & Methods:** The aims of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and pathology files of 4402 endoscopically resected specimens performed during January 2007 and December 2015 in our hospital. A total of 381 serrated lesions resected were classified into three 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 381 lesions, a total of 194 (50.9%) were HP, 77 (20.2%) SSA/P, and 110 (28.9%) TSA. Male to female ratio (M/F) was 2.35 for HP, 1.02 for SSA/P, and 2.45 for TSA. Mean size of SSA/Ps (13.1 mm) and TSAs (10.4 mm) were significantly larger than that of HP (8.5 mm) ($p < 0.005$, respectively). SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 85% 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 194), 2.6% (2 out of 77), and 4.5% (5 out of 110), 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 three 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 of Interest:** All authors have declared no conflicts of interest.

## P0367 COMPARISON OF A METHYLATED BCAT1/IKZF1 BLOOD TEST WITH CEA FOR RECURRENT COLORECTAL CANCER

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**Introduction:** Recurrence will develop in 30–50% of colorectal cancer (CRC) cases despite apparent clearance following treatment. Carcinoembryonic-antigen (CEA) is the only guideline-recommended blood test for monitoring cases for recurrence, but its sensitivity and specificity are suboptimal and its survival value might be improved upon. A more sensitive test for recurrence might provide survival benefit.

**Aims & Methods:** This study compared a novel 2-gene (methylated *BCAT1 and IKZF1* DNA) blood test to CEA for detection of recurrent CRC. To do this, we conducted an observational, paired comparison of detectable methylated *BCAT1 and IKZF1* DNA with CEA (cut-off 5 ng/mL) in blood from patients in remission after treatment for primary CRC and undergoing surveillance at 3–6-monthly intervals. Blood collected in the 12-months prior to or 3 months after radiological assessment of recurrence status were assayed and the results (in the sample collected closest to ascertainment of recurrence status) compared by McNemar's test. Recurrence status was determined by a combination of radiological, pathological and endoscopic methods.

**Results:** Of 397 patients enrolled, 220 underwent satisfactory assessment for recurrence and 122 had blood testing performed within the prescribed period. In 28 cases with recurrent CRC, CEA was positive in 9 (32%; 95%CI 16–52%) compared to 19 (68%; 95%CI 48–84%) positive for methylated *BCAT1/IKZF1* ($p = 0.002$). All samples from cases with recurrence that were CEA positive were also *BCAT1/IKZF1* positive (none was positive by CEA alone). Sensitivity estimates of the methylated *BCAT1/IKZF1* test for local ($n = 4$) and distant ($n = 24$) recurrence were 75% and 66.7%, respectively, compared to 50% and 29.2% for CEA. In 94 patients without clinically-detectable recurrence, CEA was positive in 6 (6%, 95%CI 2–13%) and *BCAT1/IKZF1* in 12 (13%, 95%CI 7–21%), $p = 0.210$, with only 1 of these being positive by both tests. *BCAT1/IKZF1* test positivity was not affected by gender or age. The odds ratio of a positive CEA test for recurrence was 6.9 (95%CI 2–22) compared to 14.4 (5–39) for *BCAT1/IKZF1*. The positive predictive values of methylated *BCAT1/IKZF1* and CEA in this population were 61.3% (42.2–78.2) and 60.0% (32.3–83.7) respectively.

| Concordance between tests<br>**Recurrence, n = 28** | | CEA | CEA |
|---|---|---|---|
| | **Result** | + | - |
| *BCAT1/IKZF1* | + | 9 | 10 |
| *BCAT1/IKZF1* | - | 0 | 9 |
| **No apparent recurrence, n = 94** | | | |
| *BCAT1/IKZF1* | + | 1 | 11 |
| *BCAT1/IKZF1* | - | 5 | 77 |

**Conclusion:** The *BCAT1/IKZF1* test was more sensitive for recurrence and picks up additional cases not detected by CEA. Also, recurrence was twice as likely with a positive *BCAT1/IKZF1* test than with CEA when applied on a single occasion. This test should be considered for monitoring cases for recurrence after induction of remission.

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S. Pedersen: Paid employee of Clinical Genomics Pty Ltd.
D. Murray: Paid employee of Clinical Genomics Pty Ltd.
R. Baker: Paid employee of Clinical Genomics Pty Ltd.
All other authors have declared no conflicts of interest.

## P0368 CARBONIC ANHYDRASE IX AS THE MARKER OF THE HYPOXIA INDUCED EXTRACELLULAR VESICLE SECRETION

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**Introduction:** Carbonic anhydrase IX (CAIX) is a hypoxia-inducible enzyme that is overexpressed in a variety of cancers including colon cancer and plays a crucial role in maintaining favourable intracellular pH and reducing extracellular pH, thus providing a selective advantage for cancer cells. There is also evidence that extracellular vesicle (EV) production is increased in response to hypoxia and promotes adaptive response of cancer cells.

**Aims & Methods:** Within this study, we explored a possibility to use CAIX for the isolation of hypoxic exosomes from colorectal cancer (CRC) patients' plasma. Colon cancer cell lines SW480 and SW620 that are originally derived from primary and metastatic tumour from a single patient were cultured under hypoxic or normoxic conditions. Exosome-enriched EV fractions were isolated from cell culture mediums and plasma samples from 12 CRC patients and 10 healthy donors by using sequential centrifugation, filtration and size-exclusion chromatography steps.

**Results:** Nanoparticle tracking analysis (NTA) of EVs produced by SW480 and SW620 cell lines showed that SW620 cells secrete 70% more EVs than SW480 cells in normoxia and hypoxia stimulates EV secretion by 80% in SW480 cells and 449% in SW620 cells. In addition, we observed changes in the size distribution of EVs produced by SW620 cells under hypoxic conditions while no such difference was observed in SW480 cells in response to hypoxia. By measuring CAIX positive EVs in cell cultures, we concluded that the CAIX positive proportion is increased by 10% in SW480 and 15% in SW620 cells in response to hypoxia. No significant differences in the amount and size distribution of EVs were observed between healthy donors and CRC patient cohorts based on NTA data. However it seems that there is a tendency that the percentage of CAIX-positive EVs increases with the stage of CRC and is higher in stage II-IV CRC patients than in healthy controls. In addition, it is higher in patients with metastasis than without distant metastases, but does not correlates with tumour size.

**Conclusion:** CAIX can be detected on the surface of EVs and the production of CAIX positive EVs is increased under hypoxic conditions suggesting that CAIX positive EVs in patients' plasma might have diagnostic or prognostic value. However it seems that possibly there is also different source of CAIX positive EVs in human plasma beside the tumour. (Financed by Latvian council of science Collaboration project No: 625/2014).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0369 OPTIMAL INTAKE OF CLEAR LIQUIDS DURING PREPARATION FOR COLONOSCOPY WITH LOW VOLUME POLYETHYLENE GLYCOL PLUS ASCORBIC ACID (PEG-ASC)

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**Introduction:** Polyethylene glycol electrolyte lavage solution containing ascorbic acid (PEG-ASC) has recently become available in Japan, as a low volume lavage solution. In a previous trial[1], we found that the 1.5-L PEG-ASC regimen had higher patient acceptability than the 2-L PEG-ELS regimen. Tolerability, bowel cleansing, and safety were similar between regimens. So, the 1.5-L PEG-ASC regimen has become a standard regimen for afternoon procedures in Japan. The regimen is sequential intake of one liter of PEG-ASC, 500 mL of clear liquid, 500 mL of PEG-ASC, and finally 250 mL of clear fluids (all at rate of 250 ml every 15 min) on the day of colonoscopy. However, the regimen seems to be intolerable and complicated for many patients, especially in elderly.

**Aims & Methods:** The aim of this study was to evaluate an alternate regimen of 500 ml of PEG-ASC followed by 250 mL clear liquids, repeated 3 times compared to the standard regimen. We conducted a single-blinded, non-inferiority, randomized, controlled study. Subjects were randomized to the standard regimen or the alternate one (UMIN000014766). The Boston Bowel Preparation Scale was used to evaluate bowel cleansing, and a 3-point scale was used to assess mucosal visibility. The primary endpoint was the rate of successful bowel cleansing. The acceptability, tolerability, safety, and endoscopic findings of these two regimens were secondary endpoints.

**Results:** Four hundred and nine patients were randomized to either the standard regimen ($n = 204$, males 54.0%, mean age 65.5 years) or the alternate regimen ($n = 205$, males 54.6%, mean age 65.0 years). The rates of successful bowel cleansing were 71.1% (64.3–77.2%) in standard regimen vs. 75.1% (68.6–80.9%) in alternate regimen (95% lower confidence limit, for the difference = -4.6, non-inferiority $P < 0.05$). No significant differences were found in the rates of 100% volume intake of each regimen (94.6% vs 96.1%; $P = 0.49$), the frequency of defecation (9.4 vs 9.3; $P = 0.61$), the time to preparation (170 min vs 168 min; $P = 0.63$), feel of nausea (4.9% vs 2.0%; $P = 0.13$), distension (27.9% vs 23.4%; $P = 0.22$), cases of vomiting (3 vs 1; $P = 0.37$), the willingness to repeat the same regimen (79.0% vs 76.7%; $P = 0.71$), polyp detection rate (57.8% vs 62.4%; $P = 0.72$), and optimal visibility grades of 0/1/2 (105/68/31 vs 118/62/25; $P = 0.17$).

**Conclusion:** The alternate regimen and standard regimen are clinically equivalent, with respect to cleansing efficacy and acceptability, tolerability, safety, and endoscopic findings. These results will give good news for patients had difficulty in drinking the first liter of PEG-ASC.

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All other authors have declared no conflicts of interest.

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## P0370 DESIGN AND EVALUATION OF A GENES PANEL FOR DIAGNOSING HEREDITARY GASTROINTESTINAL CANCER, ANALYZABLE BY NEXT-GENERATION SEQUENCING, NGS

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**Introduction:** The development of new sequencing technologies (next generation sequencing, NGS) is a paradigm shift in the study of diseases and enabling rapid and cost - effective analysis of a substantial number of genes. This tool could improve the diagnosis of hereditary forms of cancer. A panel of genes has been designed, analyzable by NGS, in order to validate it as an alternative to the diagnosis of hereditary digestive cancer strategy based on clinical criteria.

**Aims & Methods:** Twenty-one genes involved in hereditary forms of colon, stomach and pancreatic cancer have been included in the same panel (version 1: v1DIGCUN): *APC, BMPR1A, BRCA1, BRCA2, CDH1, CDKN2A, ENG, EpCAM GREM1, MLH1, MSH2, MSH6, MUTYH, PALB2, PMS2, POLD1, POLE, PRSS1, PTEN, SMAD4, SPINK1*. The panel design was made with the SureDesign (Agilent Technologies) program with coverage of all coding exons and flanking intron of 25 nt. The libraries were developed in HaloPlex (Agilent Technologies) technology and sequenced on an Ion Torrent PGM (Thermo Fisher). NGS data were analyzed with software programs and Ion Torrent Suite Reporter ™ Software. A total of 53 patients selected in the High Risk Clinic on Digestive Tumors in our hospital have been included, 10 of them with known mutation (positive controls). The identified variants were analyzed on the basis of specific gene data, ClinVar, dbSNP, Exac Genome Browser, BIC and variants of uncertain significance (VOUS) were predicted by Asessor Mutation, Mutation Taster, PolyPhen-2 and SIFT.

**Results:** All known variants in controls have been identified and validated. Twenty-nine of the 43 cases analyzed showed no mutations or VOUS, only polymorphisms. In 14 cases, 16 variants were found: 1 mutation in *PTEN* probably pathogenic (c.507_510delCAGT / p.Ser170fs) and 15 VUS (3 *APC*, 3 *POLD1, 2 POLE, 2 MSH6, 1 BRCA1, 1 BMPR1A, 1 MSH2, 1 PMS2 and 1 PALB2*). It is currently establishing the relationship between the clinical phenotype and the possible contributor to the disease gene.

**Conclusion:** We developed the first version of a genes panel, analyzable by NGS with adequate diagnostic accuracy for known mutations. They have also identified many variants not initially suspected by phenotype genes. If the pathogenicity of those variants is confirmed, this strategy could potentially improve the diagnosis of hereditary forms of digestive cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0371 POSITIVE LYMPH NODE RATIO IS A PROGNOSTIC FACTOR FOR STAGE III COLORECTAL CANCER PATIENTS WITH MUCINOUS ADENOCARCINOMA AND SIGNET RING CELL CARCINOMA

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**Introduction:** The survival rates for colorectal cancer (CRC) patients with mucinous adenocarcinoma or signet-ring cell carcinoma (Muc/Sig) are worse than for patients with differentiated adenocarcinoma (AC). In addition, previous studies have reported that a positive lymph node ratio (LNR) is a prognostic factor in CRC. However, the clinical significance of LNR in CRC patients with Muc/Sig is unclear.

**Aims & Methods:** The aim of this study was to evaluate the prognostic impact of histologic type and LNR in patients with stage III colorectal cancer. The data for stage III CRC patients, who underwent surgical curative resection between 1997 and 2006, were retrospectively collected from 22 referral institutions of the Japanese Study Group for Postoperative Follow-up of Colorectal Cancer. The patients were divided into two groups according to histologic types: (1) Muc/Sig and (2) AC. LNR was categorized as low ($<0.25$) or high ($\geq 0.25$).

**Results:** Of the 7036 patients studied, the Muc/Sig histologic type was observed in 316 patients. The disease-specific survival (DSS) and relapse-free survival (RFS) rates were worse in the Muc/Sig group than in the AC group. A multivariate analysis revealed that the incidence of Muc/Sig and high LNR were independently associated with poor DSS and RFS. In addition, the RFS rates did not differ according to the histologic type in patients with low LNR; however, for patients with high LNR, the RFS rates were worse in the Muc/Sig group than in the AC group. Therefore, we focused on stage III CRC patients with Muc/Sig. The multivariate analysis further revealed that high LNR was independently associated with poor DSS (HR = 3.252, 95% CI: 1.971–5.383, $P < 0.001$) and was the only independent factor associated with poor RFS (HR = 2.954, 95% CI: 1.829–4.785, $P < 0.001$). Furthermore, in stage III CRC patients with low LNRs, there was no difference in RFS rate according to histologic type. However, in patients with high LNRs, the RFS rate was worse in those with Muc/Sig than in those with AC (5-year RFS rate of the patients with low LNRs: 70.8% in the Muc/Sig group vs. 72.8% in the AC group, $P = 0.08$; patients with high LNRs: 31.5% in the Muc/Sig group vs. 53.4% in the AC group, $P < 0.001$).

**Conclusion:** We found a strong correlation between high LNR and poor prognosis in stage III CRC patients with Muc/Sig. Further studies are necessary to elucidate the effects of histologic type and LNR variations in patients with CRC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0372 KNIFE - ASSISTED SNARE RESECTION (KAR) PROCEDURE TIME FOR COLONIC DYSPLASTIC LESIONS AND ASSOCIATED PROGNOSTIC FACTORS

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**Introduction:** The combination of endoscopic knife and snare, known as Knife-Assisted snare Resection (KAR) is a novel technique which could be promising in the management of the colonic dysplastic lesions. KAR is a recently described effective technique to treat complex LST (Lateral Spreading Tumors). It involves knife-assisted circumferential mucosal incision followed by some submucosal (SM) dissection before snare assisted resection. Depending on the degree of SM dissection and lesion size a single or multiple piece resection is achieved. It is much safer then ESD and has better outcome than EMR in the west. However, detailed evaluation of the time spent for every part of this procedure and the possible factors which can affect it, is rather limited.

**Aims & Methods:** Aims: To establish individual component steps of KAR procedure and identify the time taken for each step of the KAR. Secondary aim was to identify factors influencing the procedure time. Patients and Methods 42 consecutive patients were enrolled in this study. All the endoscopic procedures have been performed by a single experienced endoscopist (PB), have been recorded in full on a video recorder and were analyzed by an independent researcher with experience in KAR procedure. First 50 patients who had KAR were excluded from this study as a part of learning curve and not analyzed. Lesion area was calculated based on length of the lesion and the percentage of the colonic circumference involved. Using the equation area = $2*\pi*$ r * l *% circumferential involvement / 100. Here r = radius (cm) and l = length of lesion. The following time of every part of the procedure was recorded: Lesion evaluation, suction/drying time, submucosal injection, mucosal incision, submucosal dissection, snaring, accessory change times, post resection evaluation, hemostatic (blood control) time and total procedural time.

**Results:** The mean age of the patients was 57 ± 28 years. The mean size of the lesion was 40 mm (range 15 mm -100 mm) with a mean area of 7.53 $cm^2$ (range: 4.71–14.13 $cm^2$), whereas the mean circumferential percentage was 42%. The morphology of the lesion was LST (Lateral Spreading Tumors) from which 43% was resected enbloc. Complete endoscopic resection achieved in 97.75% of the cases. The mean procedural time was 95 (±54) min, equating to 12.61 min/$cm^2$.

The time taken for each component of the procedure is shown in Table 1. The lesion resection time (mucosal incision, submucosal dissection and snaring) was just under 1/3 of the total time (30%). The submucosal injection time was 16.3% while the initial evaluation of the lesion was 6% and post resection evaluation was 14.6%. Bleeding control took 3.2% of the total time. The time recorded for accessory change, suction/drying and lumen insufflation time was 32%. Circumferential extension seemed to affect the total procedure time, with $<50\%$ circumference lesions taking 72 min versus 122 min for lesions with $>50\%$ circumferential extension. ($p = 0.0067$) Procedural time was also significantly influenced by lesion size. For colonic lesions $>40$ mm the mean time was 125.65 min whereas for the lesions $<40$ mm the mean time was 60.32 min. ($p = 0.0018$)

**Table 1. Time recorded for each component of the KAR procedure**

| Time recording | MeanTime (min) ± SD | Percentage (%) |
|---|---|---|
| Initial Lesion Evaluation | 6.28 (±4.29) | 6% |
| Submucosal Injection Time | 15.57 (± 10.38) | 16.3% |
| Resection Time (Mucosal incision, Submucosal Dissection, Snaring) | 29.35 (±29.31) | 31% |
| Post Resection Evaluation | 8.23 (± 5.46) | 8.5% |
| Accessory Change Time/ drying / Lumen Insufflation | 30.37 (± 30.39) | 31% |
| Blood Control (hemostatic) Time | 3.04 (±5.34) | 3.2% |
| Other | 4.21 (± 2.37) | 4% |
| Total | 95.27 (±54.27) | 100% |

**Conclusion:** Our data showed that it takes 12.61 min/$cm^2$ to perform KAR for LST lesions in colon. Size of the lesion as well as circumferential extent seems to

be the predictors of the procedural time. Only one third of the total procedure time was spent in lesion resection. Another third of time was spent in inflating & deflating the lumen and changing accessories. We believe that this data can help influence future research in improving KAR procedure times &comparing new devices for KAR & ESD. This data will also help clinicians allocate appropriate time for procedures and remuneration for the procedure.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0373 A COMPARATIVE STUDY FOR EFFECTIVENESS OF IRREVERSIBLE ELECTROPORATION ABLATION ACCORDING TO THERAPEUTIC METHOD AND PERIOD: COLON CANCER ANIMAL MODEL

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**Introduction:** Irreversible electroporation (IRE) is a promising novel technique for the ablation of tumor. IRE has an advantage over other ablation technique in its mechanism to remove undesired cells by affecting the cell membrane without thermally destructing surrounding blood vessels, nerves. There have been recent concerns regarding the potential use of IRE as an ablative modality. The aim of this study was to evaluate the effectiveness of IRE ablation according to therapeutic method in colon cancer animal model.
**Aims & Methods:** Male nude mice (6 weeks old) were introduced. Caco2 cells (ATCC) were each visually injected into both flakes. We performed in vivo IRE procedures in the tumors of nude mouse model. Electrical pulses were applied to the tumor of nude mice using a DC generator at $1 \sim 2\,kV/cm$ amplitude, $100 \sim 200$ pulses, $100 \sim 300\,\mu s$ length. A group received early ablation (0, 7 day), and the other group received continuous ablation (0, 7, 14, and 21 days). We compared the size of tumors between control and IRE ablation group.
**Results:** The size of IRE ablative tumors significantly decreased comparing with the control. ($p = 0.005$) But there was no significant difference between early ablation group and continuous ablation group. ($p = 0.972$) There was complete cell death within the IRE lesions without intervening live cells. Histologically, in each group, the IRE ablative tumors were nonviable, with a persistent tumor nodule replaced fibrosis. The tissue with H&E stain and Tunnel assay showed apoptotic cell death in the 1 days after IRE ablation. The tissues after 24 hr IRE ablation showed diffuse necrotic cell death.
**Conclusion:** The present study demonstrated that IRE ablated colon cancer tissue very effectively through the induction of cellular apoptosis in the early stage. This study suggests that IRE is the potential use of IRE in colon cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0374 IDENTIFICATION OF PROTEOMIC PROFILES ASSOCIATED WITH TUMOR REGRESSION GRADING IN RECTAL CANCER

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**Introduction:** Rectal cancer response to neoadiuvant chemo-radiotherapy (CRT) is variable. Identifying markers of response will help select patients more likely to benefit from therapy. Objective of the study is to identify at diagnosis proteomic profiles associated with tumor regression grading (TRG) in rectal cancer.
**Aims & Methods:** This study includes 41 patients with rectal cancer treated with CRT followed by surgery. Proteins from pre-treatment tumor biopsies and control from paired normal bioptic specimens were screened for comparative proteomic approach by using 2D difference gel electrophoresis (2D-DIGE). Differential spots found with Decyder were identified by MALDI-TOF and peptide fingerprinting with Mascot search engine. Interactions among identified proteins was analysed with STRING 9.1 search tool. Pathological TRG was assessed on surgical specimens.
**Results:** A total of 30 proteins were identified as discriminators between tumor samples and controls by principal component analysis and hierarchical clustering ($p < 0.01$; spot map $> 50\%$). These proteins were already described as involved in rectal metabolic cell pathways and angiogenesis. Possible correlations between these proteins and TRG are under evaluation.
**Conclusion:** Comparative proteomics approach based on 2D-DIGE and MALDI-TOF identification succeeded in differentiating rectal tumor samples from paired normal rectal mucosa. Further analyses will unravel possible correlations between distinct protein profiles and TRG response to CRT treatment that could be used to select optimal therapy in rectal cancer patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0375 COLORECTAL CANCER IN THE ELDERLY – HOW MUCH SHOULD WE INVEST?

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**Introduction:** Colorectal cancer (CRC) treatment in elderly patients gains complexity due to the frequently associated comorbidities. The influence of seniority in prognosis and therapy safety is not evaluated in clinical trials, making its study in the clinical practice an essential tool.
**Aims & Methods:** To determine the impact of age $\geq 80$ years in the therapeutic management and outcome of patients with CRC. Single-center cohort study of patients aged $\geq 80$ years at CRC diagnosis, evaluated in a Multidisciplinary Group, between January/2010 and December/2012, and followed prospectively. Analysis of clinical characteristics, TNM stage, therapeutic decision and evolution. Statistics: Fisher's exact test, Kaplan-Meyer (SPSS-21).
**Results:** 108 patients were evaluated, 59.3% male, mean age $83.4 \pm 2.97$ years (80–94). Most of the patients presented a performance status 0–1 (90.7%) and a Charlson comorbidity index $2.05 \pm 2.71$. The CRC diagnosis was established in the context of symptoms in 94.4% of the patients. Location: rectum 43.5%; colon 50.9%; synchronous tumours 5.6%. Stages III-IV in 58.3%. 80.6% of patients were proposed for curative intent (CI) therapy, from which 82% (71/87) completed the treatment. The presence of stage IV disease at diagnosis was associated with palliative intent (PI) therapy decision ($p < 0.001$). There were 9 deaths secondary to therapy: 8 postoperatively; 1 by chemotherapy – significant association with PI therapy ($p = 0.037$). Postoperative mortality was significantly associated with PI therapy ($p = 0.001$) but not with age $\geq 85$ years ($p = 0.23$). Survival of patients proposed for CI therapy: 71.8% and 45.8%, in the first and third years, respectively. CI therapy was significantly associated with a higher overall survival ($p < 0.001$).
**Conclusion:** CRC among patients aged $\geq 80$ years was mainly diagnosed in advanced stages, limiting therapeutic options. Still, PI therapy was found to be associated with higher mortality from complications - therefore, the CI therapy investment should not be restricted by age.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0376 COMPARISON OF ENDOSCOPIC SUBMUCOSAL DISSECTION OUTCOME IN OUTPATIENTS VERSUS INPATIENTS

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**Introduction:** Endoscopic submucosal dissection (ESD) is worldwide accepted as a minimally invasive treatment for early gastrointestinal (GI) cancer but it is still considered a challenging and risky procedure in the colorectum. In both Eastern and Western settings published studies indicate that the vast majority of patients undergoing ESD are hospitalized because of the expected high risk of complications.

**Aims & Methods:** Aim of this study is to investigate the efficacy and safety of colorectal ESDs performed in outpatient setting, in a tertiary center. From May 2014 to March 2016, all consecutive patients treated at Humanitas Research Hospital, Italy for colorectal ESD were enrolled in a prospective registry. Per protocol patients > 80 years and with comorbidities (ASA III) were admitted in hospital for at least two nights, whereas ESD was performed in outpatient setting in the remaining patients. Complete resection rate (R0) and major complications (perforation, immediate bleeding - defined as a large amount of bleeding during the procedure and/or difficult hemostasis - and delayed bleeding -defined as clinical evidence of melena within 10 days after the procedure that required endoscopic treatment-) were compared using Fisher exact test for categorical variables. All differences were considered significant at two-sided p-values $< 0.05$.

**Results:** A total of 107 (M/F 71/36, mean age 66.8 years) consecutive patients were treated by ESD for 108 colorectal lesions (rectum 59.2%, left colon 13.8%, transverse colon 10.2%, right colon 16.6%). All procedures were performed under deep sedation (propofol i.v.) administered by a dedicated anaesthesiologist; none of the patients required general anaesthesia. The median operation time was 85.4 (range 15–293) minutes and the mean size of resected specimens was 39.7 mm (range 12–120 mm). Thirty-nine patients were hospitalized (36.1%) whereas 69 (63.9%) were treated as outpatients. Complete resection rate was 97.4% in inpatient group and 98.5% in outpatient group ($p = ns$). Perforations occurred in 3 cases (2.8%): 2 in the inpatient group (5.12%) and 1 in the outpatient group (1.5%) ($p = ns$). All of them were endoscopically treated. No immediate nor delayed bleeding occurred.

**Conclusion:** Endoscopic submucosal dissection is a feasible technique to treat superficial colorectal tumors with a high resection rate and low complication rate. It is safe and effective not only for hospitalized patients but also in an out-patient setting. Although a cost-effective analysis was not performed, we could speculate that outpatient setting could lead to minor costs and minor patients discomfort than inpatient setting.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0377 THE VALIDITY OF THREE STEPS LEARNING SYSTEM OF COLORECTAL ESD

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**Introduction:** Endoscopic submucosal dissection (ESD) for early colorectal tumors has become a widespread treatment, but still have technical difficulties. A standard training system for colorectal ESD remains to be established. We reported, in UEG week last year, our original training program called three steps learning system (TSLS), and the trainee has gained more experience. Now, TSLS is considered to be verified again in terms of the safety and validity.

**Aims & Methods:** TSLS consists of the following qualifications. The trainee (A) has experienced 1000 upper/300 lower endoscopy, 30 gastric ESD, and 20 colorectal ESD assistance. Colorectal ESD is performed with support by an expert (B) under the 3 steps. 1) 0–5 cases: the position is all rectum, and have no fibrosis (F0), 2) 6–20cases: tumor size is $\leq$50 mm with no or mild fibrosis (F0/F1) and the expert gives every possible advices during procedures, 3) 21cases-: The expert gives important advices or hands-on support when needed. 262 consecutive ESD procedures performed in Omori Red Cross Hospital from 2012 April to 2016 March were retrospectively analyzed. We evaluated clinical backgrounds, treatment outcomes, complications, and postoperative courses. We aimed to evaluate the safety and validity of TSLS.

**Results:** A/B performed 49/169 cases respectively (44 cases were performed by another endoscopist). The mean age, sex, comorbid diseases (hypertension, diabetes, renal dysfunction, cardiac disease), rate of having antithrombotic agents were similar between two groups. Tumor locations were C3/A7/T12/D5/S8/R14 in group A and C25/A35/T36/D18/S21/R34 in group B ($p = 0.43$). The trainee tended to perform more rectal lesion and less cecal lesions. Protruded tumors were 1 case (2.0%) in A and 12 cases (7.1%) in B. There were also no significant differences in specimen size, tumor size, en bloc resection rate, and complication: $38.3 \pm 18.1$ mm, $26.4 \pm 16.3$ mm, 100%, and 1 case (perforation) in group A and $37.8 \pm 16.5$ mm, $29.6 \pm 15.9$ mm, 99.4% (168/169), and 1 case (perforation) in group B, respectively. Only an operation time and speed of resection (specimen size ($mm^2$) / operation time (min)) in group B were much faster than group A: $59.0 \pm 43.1$ min, $17.0 \pm 8.4 mm^2$/min in group A and $35.5 \pm 36.2$ min, $33.1 \pm 17.1 mm^2$/min ($p < 0.01$). The rate of fibrosis was 12.2% (F0/F1/F2: 43/6/0) in group A, 22.5% (F0/F1/F2: 131/33/5) in group B ($p = 0.22$). Trainee's self-completion rate was 83.7% (41/49) (85% (17/20) in the initial 20 cases and 82.8% (24/29) in subsequent 29 cases). The most frequent reason for not self-completion was difficulty in technique or hemostasis. R0 resection rate were similar, 95.9% (47/49) in group A, and 95.3% (161/169) in group B. The clinical courses after procedures (fever, WBC, CRP) were also similar.

**Conclusion:** Under our training system (TSLS), through the support by an expert and selection of the lesion for the initial 20 cases, it might be possible that the trainee can gradually become able to perform colorectal ESD by himself. TSLS was considered to be an effective and safe method. We need to attempt this training system to other novices and verify the validity of our system.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0378 ANGIOGENESIS INHIBITOR-RELATED ANAL CANAL ULCERS IN METASTATIC COLORECTAL CANCER PATIENTS

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**Introduction:** Combining conventional systemic chemotherapy with the angiogenesis inhibitor bevacizumab is now recommended as a first treatment for metastatic colorectal neoplasms. The risk for short-term postoperative complications related to bevacizumab has been assessed but anal canal ulcers related to angiogenesis inhibitors have never been described.

**Aims & Methods:** The aim of our study was to assess the prevalence of angiogenesis inhibitor-related anal canal ulcers in colorectal cancer patients and its impact on patient wellness and therapy.

We reviewed a cohort of 404 consecutive patients undergoing chemotherapy for metastatic colorectal cancer from january 2010 to december 2013. In this cohort 333 patients had at least one angiogenesis inhibitor and 71 had other chemotherapy regimens.

Details about patients history, therapy protocols, and proctology reports were retrived. Pain was graded in a semiquantitative scale (0–3) where higher is more severe.

Vascularizaton of anal canal was compared with contrast MRI in patients with angiogenesis inhibitor and in healthy controls.

Non parametric statistics was performed.

**Results:** In the study period, twenty five patients, among the 404 ones, were referred to the proctology outpatient clinic for perianal complaints. Ten patients (3.0%) experienced an anal ulcer while in therapy with angiogenesis inhibitor while only a patient (1.4%) treated with other chemoterapy regimens had one [OR = 2.1 (95% CI 0.273–17.2)]. The pain intensity was medianly severe (3 IQR:2-3). The risk of having the chemotherapy interrupted or suspended for perianal disorders was higher while on therapy with angiogenesis inhibitor [OR = 2.8 (95% CI 0.366–22.1)]. Vascularizaton of anal canal, as measured with relative contrast enhancement at MRI, was signifcantly lower in patients with angiogenesis inhibitor than in healthy controls ($p = 0.03$).

**Conclusion:** Angiogenesis inhibitors-related anal canal ulcers in colorectal cancer patients are a rare complication that can compromise the prosecution of the life saving therapy. A low vascularization of the anal canal mucosa due to angiogeneisis inhibitor subministration is possibly involved in the pathogeneisis of this complication. Adequate strategies should be implemented to prevent this complication.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0379 PARTHENOLIDE ENHANCES ANTI-TUMOR EFFICACY OF BALSALAZIDE IN HUMAN COLON CANCER CELLS AND COLITIS-ASSOCIATED COLORECTAL CANCER BY BLOCKADE OF NF-KB ACTIVATION

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**Introduction:** Balsalazide is a colon-specific prodrug of 5-aminosalicylate (5-ASA) that was recently shown to be associated with a reduced risk of colon cancer in patients with ulcerative colitis. Parthenolide (PT), a strong NF-kB inhibitor, has recently been demonstrated to be a promising anticancer agent that promotes apoptosis of cancer cells.

**Aims & Methods:** In the present study, we investigated the antitumor effect of balsalazide combined with PT through inhibition of nuclear factor-kB (NF-kB) activation in human CRCs.

**Results:** Our results demonstrated that the combination of balsalazide and PT markedly suppressed proliferation, nuclear translocation of NF-$\kappa$B, I$\kappa$B-a phosphorylation, NF-kB DNA binding and expression of NF-kB target proteins. Apoptosis under NF-kB signaling was confirmed by detecting expression of caspases, p53 and PARP. Moreover, treatment of a colitis-associated colon cancer (CAC) murine model with PT and balsalazide resulted in significant recovery of body weight and improvement in histological severity. Administration of PT and balsalazide to CAC models also suppressed carcinogenesis as demonstrated by uptake of $^{18}$F-fluoro-2-deoxy-D-glucose (FDG) using micro PET/CT scans.

**Conclusion:** These results demonstrate that PT potentiates the efficacy of balsalazide through synergistic inhibition of NF-kB and the combination of dual agents prevents colon carcinogenesis from chronic inflammation. This is the first evidence that a combination of balsalazide and PT could be a new regimen for colorectal cancer treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0380 EFFICACY OF PREOPERATIVE COLONOSCOPIC TATTOOING ON LYMPH NODE HARVEST

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**Introduction:** Consensus guidelines suggest to assess at least 12 lymph nodes for adequate staging of colorectal cancer and thecorrelation between number of lymph nodes retrieved and the patient survival has been formerly reported. To facilitate the retrieval of lymph nodes, preoperative endoscopic tattooing to mark the site of the tumor has been proposed.
**Aims & Methods:** In the study, we aimed to identify the impact of preoperative colonoscopic tattooing (PCT) on lymph node harvest incolorectal cancer patients. 682 patients who underwent curative resection for colorectal cancer between 2013 and 2015 at the Pusan NationalUniversity Yangsan Hospital in Korea were retrospectively divided into the tattooing group and the non-tattooing group depending on whether preoperative indocyanine green (ICG) tattooing was done. Pathological findings and lymphnode harvest were compared between the two groups. For the same stage comparison, lymph nodes harvest of T1stage colorectal cancer patients in the two groups were compared.
**Results:** The median number of lymph nodes obtained was 20 in the tattooing group (N = 93) and 23 in the non-tattooing group (N = 589). The rate of adequate lymph node harvest (retrieval of more than 12 lymph nodes) was higher in the non-tattooing group than that in the tattooing group (93.3% vs. 89.2%). As for the same stage comparison (T1 stage) therewere 48 patients in the tattooing group and 51 patients in the non-tattooing group. The median number of lymphnodes obtained was 20 in the tattooing group and 21 in the non-tattooing group. The rate of adequate lymph nodeharvest was also higher in the non-tattooing group (89.6 vs. 86.3%).
**Conclusion:** PCT did not have any association with higher lymph node yield in colorectal cancer. Further studies are needed todetermine if preoperative colonoscopic tattooing to mark the tumor site is related to better lymph node yield.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0381 DEFECATORY SYMPTOMS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME IN A PRIMARY HEALTH CARE POPULATION IN SWEDEN

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**Introduction:** Irritable bowel syndrome (IBS) is a chronic disorder characterized by abdominal pain and alterations in bowel habits (diarrhoea, constipation, or both in an alternating pattern) that affects approximately 10% of the general population. IBS is associated with impaired quality of life and increased use of health care resources[1]. The majority of patients are diagnosed and treated in primary care[2]. Many IBS patients suffer from symptoms related to defecation, such as the feeling of incomplete evacuation or straining, but the prevalence of these symptoms has not yet been well described in a primary care setting.
**Aims & Methods:** The aim was to characterize and compare defecation symptoms in patients with IBS in a primary health care population. The study adopted a case-control design in a defined region in south-east Sweden (i.e., the County Council of Östergötland). Patient recruitment was accomplished in 10 Primary Health Care (PHC) centres located in the 3 major cities of the region during March 2010 and February 2014. These PHC centres are responsible for the primary care of approximately 150 000 inhabitants (≈1/3 of the region). For this study, patients within the normal working age range (18–65 years) with a clinical IBS diagnosis and active symptoms during the last 2 years, identified with ICD-10 diagnoses in the patient medical register, were invited by e-mail to participate. IBS patients meeting the ROME III criteria were included (n = 282). The control group was comprised of other patients at the selected PHC centres who were similar in terms of sex and age, and sought care for complaints not associated with gastrointestinal symptoms and with no earlier gastrointestinal diagnoses found in the patient register for the previous 2 years (n = 372). Subjects recorded their bowel habits and symptoms prospectively on validated diary cards[3] for 2 weeks. They were asked to record every single stool, stool consistency, and corresponding defecatory symptoms: urgency, straining, and feeling of incomplete evacuation. Stool consistency was defined by the Bristol Stool Form Scale. IBS and control groups were statistically compared with respect to occurrence of defecatory symptoms using unconditional logistic regression (symptom prevalence) or proportional odds models (number of simultaneous symptoms per bowel movement). All statistical tests and confidence intervals adjusted variance estimates for multiple observations per patient via the intraclass correlation.
**Results:** During the 2-week recording the total number of stools was 6785 in IBS patients and 6635 in controls. The feeling of incomplete evacuation, straining and urgency associated with defecation were more present in patients with IBS than controls ($p < 0.001$; $p = 0.002$; $p < 0.001$) (Table 1). The feeling of incomplete evacuation was present in 49% of the stools among the IBS patients and in 21% of the stools among the controls. The need of straining during defecation was reported in 41% of stools by IBS patients compared to 33% of the stools by controls. Urgency was experienced in 37% of the stools in IBS patients compared with 18% in controls. Patients with IBS experienced to a higher degree more than one defecatory symptom per stool (OR 3.51, 95% CI 2.81–4.38; $p < 0.001$) (Table 1).

**Table 1:** Logistic regression analyses comparing IBS patients with controls in terms of odds of urgency, straining and feeling of incomplete evacuation associated with defecation.

| | OR (95% CI) | p-value |
|---|---|---|
| Feeling of incomplete evacuation | 3.63 (2.81–4.69) | <0.001 |
| Need to strain during defecation | 1.45 (1.15–1.83) | 0.002 |
| Experiencing urgency | 2.77 (2.11–3.63) | <0.001 |
| Number of symptoms per bowel movement | 3.51 (2.81–4.38) | <0.001 |

OR: odds ratio; 95% CI: confidence interval.
**Conclusion:** To our knowledge this is the first time defecatory symptoms are investigated for IBS patients in a primary care setting. The IBS patients experienced more defecatory symptoms such as straining, urgency and feeling of incomplete evacuation, than the primary care patient population without IBS. Patients with IBS were also more frequently experiencing more than one defecatory symptom per stool.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0382 IMPACT OF IRRITABLE BOWEL SYNDROME WITH DIARRHOEA ON WORK PRODUCTIVITY AND DAILY ACTIVITY AMONG PATIENTS IN THE EU5

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**Introduction:** Irritable bowel syndrome (IBS) is one of the most commonly diagnosed gastrointestinal disorders. IBS is subtyped based on the predominant stool pattern, with the diarrhoea-predominant subtype (IBS-D) accounting for 30–40% of all cases. IBS symptoms significantly impact patients' work productivity and activities of daily living, resulting in a substantial burden for both patients and employers. As the symptoms of IBS differ between subtypes, an understanding of the impact of each subtype is important; however, European data specific to IBS-D are lacking.
**Aims & Methods:** The objective of this study was to assess the impact of IBS-D on work productivity and daily activity impairment. Adult IBS-D patients from the EU5 (Spain, France, Italy, Germany, United Kingdom) were identified from the 2013 National Health and Wellness Survey, a self-administered, internet-based survey. Respondents were defined as diagnosed IBS-D patients if they self-reported a physician diagnosis of IBS-D, and as undiagnosed IBS-D patients if they reported experiencing IBS-D symptoms but did not self-report a physician diagnosis. Controls included all respondents without IBS (diagnosed or undiagnosed) or inflammatory bowel disease. IBS-D severity was evaluated based on a single item assessing disease severity (mild, moderate, or severe). The Work Productivity and Activity Impairment Questionnaire: General Health version assessed absenteeism, presenteeism, overall work productivity loss (absenteeism + presenteeism), and daily activity impairment in the previous 7 days. Each domain is calculated as a percentage with higher scores indicating greater impairment. Descriptive statistics were conducted to examine sample characteristics. Days of work missed annually (for employed respondents) was calculated based on reported work hours missed assuming a 40-h work week and 50 weeks worked. Bivariate analyses were used to compare work productivity and activity impairment by IBS-D severity. To assess the burden of IBS-D specifically, multivariable generalised linear models were used to compare impairment across groups, controlling for demographic and health characteristics, including age, gender, and comorbidities.
**Results:** In total, 58, 161 respondents were included (859 diagnosed IBS-D; 370 undiagnosed IBS-D; 56, 932 controls). Patients (diagnosed and undiagnosed) with severe IBS-D reported significantly greater activity impairment (n = 110; mean = 52.4%) compared with those with moderate (n = 499; mean = 38.1%) and mild (n = 620; mean = 29.5%) IBS-D ($p < 0.05$ for all). Patients with severe IBS-D also had a significantly lower rate of labour force participation (48.2%) compared with those with moderate (64.5%) or mild (67.4%) IBS-D ($p < 0.05$). After adjusting for covariates, diagnosed and undiagnosed IBS-D patients reported significantly greater lost productivity at work (presenteeism), overall work impairment, and activity impairment compared with controls (Table).

**Abstract No: P0382**
**Table.**

| Adjusted mean (SE) | Diagnosed IBS-D (n = 859) | Undiagnosed IBS-D (n = 370) | Controls (n = 56,932) | p-value: Diagnosed vs. controls | p-value: Diagnosed vs. undiagnosed | p-value: Undiagnosed vs. controls |
|---|---|---|---|---|---|---|
| Absenteeism (%) | 6.39 (1.13) | 6.01 (1.49) | 4.87 (0.10) | 0.13 | 0.40 | 0.40 |
| Presenteeism (%) | 22.45 (1.63) | 20.31 (2.09) | 15.39 (0.13) | **<0.001** | 0.43 | **0.007** |
| Overall work impairment (%) | 26.22 (1.85) | 24.33 (2.41) | 18.57 (0.15) | **<0.001** | 0.54 | **0.007** |
| Activity impairment (%) | 31.98 (1.32) | 28.47 (1.80) | 22.38 (0.11) | **<0.001** | 0.12 | **<0.001** |
| Work missed annually (days) | 15.59 (2.99) | 11.94 (3.26) | 11.25 (0.25) | 0.09 | 0.42 | 0.83 |

**Conclusion:** Compared with controls, patients with IBS-D have significantly greater impairments in work productivity and daily activities, highlighting the significant burden of illness associated with this condition. The negative impact of IBS-D on patients' daily lives is greatest for those reporting moderate or severe IBS-D.
**Disclosure of Interest:** C. Tucker: Catherine Tucker is an employee of Allergan plc.
J.L. Abel: Jessica L. Abel is an employee of Allergan plc and owns stock/stock options in Allergan plc.
R. T. Carson: Robyn T. Carson is an employee of Allergan plc and owns stock/stock options in Allergan plc.
N.M. Flores: Natalia M. Flores is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.
R. Liebert: Ryan Liebert is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.

## P0383 HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHOEA

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**Introduction:** Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by recurring abdominal pain and altered bowel habits. IBS is a common disorder, affecting approximately 10–15% of adults. The symptom burden experienced by patients with IBS is associated with significant reductions in health-related quality of life (HRQoL), though information specific to the diarrhoea-predominant subtype (IBS-D) is lacking internationally.
**Aims & Methods:** The objective of this study was to assess the impact of IBS-D on HRQoL among a sample of adults in the EU5 (Spain, France, Italy, Germany, United Kingdom). IBS-D patients were identified from the 2013 National Health and Wellness Survey, a self-administered, internet-based survey. Respondents defined as diagnosed included those who reported a physician diagnosis of IBS-D; those identified as undiagnosed reported experiencing IBS-D symptoms but did not self-report a physician diagnosis. Controls included all respondents without IBS (diagnosed or undiagnosed) or inflammatory bowel disease. IBS-D severity was evaluated based on a single item assessing disease severity (mild, moderate, or severe). HRQoL was assessed via the Short Form Health Survey version 2, scored as physical and mental component summary scores (PCS, MCS; range 0–100), and the Short Form-6 Dimension (SF-6D) score, a health utility ranging from 0 (death) to 1 (perfect health). Descriptive statistics were conducted to examine sample characteristics. Bivariate analyses (one-way ANOVA for continuous variables and chi-square tests for categorical variables) were used to compare HRQoL by IBS-D severity. Multivariable generalised linear models were used to compare diagnosed and undiagnosed patients and controls, controlling for demographic and health characteristics, including age, gender, and comorbidities.
**Results:** A total of 58, 161 respondents were included: 859 diagnosed IBS-D, 370 undiagnosed IBS-D, and 56, 932 controls. Mean age was 47 years, and 52.6% of respondents were female. HRQoL differed significantly based on self-reported IBS severity. Unadjusted comparisons showed IBS-D patients (diagnosed and undiagnosed) with moderate IBS-D (n = 499) had significantly lower HRQoL compared with those with mild IBS-D (n = 620) for MCS (40.1 vs. 43.5), PCS (47.7 vs. 50.0), and SF-6D (0.64 vs. 0.68) [all $p < 0.05$]. Similarly, patients with severe IBS-D (n = 110) had significantly lower scores (MCS, 34.9; PCS, 43.1; SF-6D, 0.57) compared with patients with moderate and mild IBS-D. Compared with controls, patients with diagnosed and undiagnosed IBS-D had significantly lower HRQoL, based on MCS, PCS, and SF-6D scores, even after controlling for demographic and health characteristics (Table).

**Table.**

| Adjusted mean (SE) | Diagnosed IBS-D (n = 859) | Undiagnosed IBS-D (n = 370) | Controls (n = 56, 932) | p-value: Diagnosed vs. controls | p-value: Diagnosed vs. undiagnosed | p-value: Undiagnosed vs. controls |
|---|---|---|---|---|---|---|
| MCS | 41.98 (0.34) | 42.44 (0.52) | 46.65 (0.04) | **<0.001** | 0.454 | **<0.001** |
| PCS | 48.83 (0.27) | 50.33 (0.41) | 51.52 (0.03) | **<0.001** | **0.002** | **0.004** |
| SF-6D | 0.66 (0.004) | 0.67 (0.007) | 0.72 (0.001) | **<0.001** | 0.277 | **<0.001** |

**Conclusion:** IBS-D patients, both diagnosed and undiagnosed, had significantly lower HRQoL in comparison with controls. Notably, HRQoL scores were significantly worse for patients with moderate or severe IBS-D than for those with mild IBS-D. The significant impact of IBS-D on patients' HRQoL emphasises the need for treatments to more effectively manage IBS-D symptoms.
**Disclosure of Interest:** C. Tucker: Catherine Tucker is an employee of Allergan plc.
J.L. Abel: Jessica L. Abel is an employee of Allergan plc and owns stock/stock options in Allergan plc.
R. T. Carson: Robyn T. Carson is an employee of Allergan plc and owns stock/stock options in Allergan plc.
N.M. Flores: Natalia M. Flores is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.
R. Liebert: Ryan Liebert is an employee of Kantar Health, which was contracted by Allergan plc for work relating to this study.

## P0384 IS THERE AN ASSOCIATION BETWEEN SELF-REPORTED ALLERGIC CONDITIONS AND FUNCTIONAL GASTROINTESTINAL DISORDERS? A POPULATION-BASED STUDY

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**Introduction:** Atopy has been associated with functional gastrointestinal disorders including irritable bowel syndrome (IBS) and functional dyspepsia (FD), implicating a shared pathophysiology.[1, 2].
**Aims & Methods:** In a population-based study we aimed to determine if allergic conditions are more common among people with FD and IBS including the subtypes of diarrhoea-predominant IBS (IBS-D) and post-infectious IBS (PI-IBS) compared with constipation-predominant IBS (IBS-C). A total of 3576 people (mean age 58.5 years, age range 18–100 years and 47.6% males) randomly selected from the Australian population returned a mail survey (response rate-= 43.6%). The survey contained self-reported questions on whether the participant had ever been told by a doctor that they had asthma, food allergy, pollen allergy and/or animal allergy. FD and IBS including constipation-predominant and diarrhoea-predominant IBS were diagnosed according to modified Rome III criteria. Post infectious IBS was defined by the history of gastroenteritis in the 3 months preceding the onset of symptoms.
**Results:** Among the general population 25.5, 4.5%, 6.7%, 2.6% and 14.6% met criteria for IBS, IBS-C, IBD-D, PI-IBS and FD respectively. One fifth of those with IBS and FD had self-reported asthma. Asthma was significantly associated with IBS (including IBS-C, IBS-D and P-IBS) and FD (Table 1). Food allergies were reported in 9% of people with IBS and 10.5% with FD and were significantly associated with IBS and FD, except PI-IBS. A pollen allergy was significantly associated with IBS including IBS-C and IBS-D but not PI-IBS or FD (Table 1). Animal allergies were less common, affecting 5.7% of people with IBS and was only significantly associated with IBS not its subgroups or with FD. In a multivariate model that included all the allergic conditions, self reporting asthma (OR = 1.45; 95%CI 1.19, 1.78, $P < 0.001$), food (OR = 1.45; 95%CI 1.08, 1.95, $P = 0.02$) and pollen (OR = 1.47; 95%CI 1.12, 1.93, $P = 0.006$) allergies were independently associated with IBS. In FD both asthma (OR = 1.46; 95%CI

1.15, 1.84, P = 0.002) and food allergies (OR = 1.79; 95%CI 1.29, 2.47, P = 0.002) were independent predictors.

Univariate associations of allergic conditions and IBS and FD.

| Self reportedallergic conditions (yes) | IBS Yes n (%) vs. No n (%) CI (95%CI) P value | FD Yes n (%) vs. No n (%) CI (95%CI) P value |
|---|---|---|
| **Asthma** | 189 (21.3)<br>373 (14.4)<br>1.61 (1.33, 1.96)<br>P < 0.001 | 112 (21.8)<br>457 (15.3)<br>1.55 (1.23, 1.95)<br>P < 0.001 |
| **Food Allergy** | 81 (9.1)<br>142 (5.5)<br>1.73 (1.31, 2.30)<br>P < 0.001 | 54 (10.5)<br>171 (5.9)<br>1.94 (1.41, 2.68)<br>P = 0.001 |
| **Pollen Allergy** | 100 (11.3)<br>172 (6.6)<br>1.79 (1.38, 2.31)<br>P < 0.001 | 49 (9.6)<br>223 (7.5)<br>1.31 (0.95, 1.81)<br>P = 0.1 |
| **Animal Allergy** | 51 (5.7)<br>87 (3.3)<br>1.81 (1.26, 2.57)<br>P < 0.001 | 23 (4.5)<br>115 (3.8)<br>1.17 (0.74, 1.86)<br>P = 0.5 |

**Conclusion:** Allergic conditions are associated with IBS including its subgroups and FD in the general population. Asthma and food allergies in particular are risk factors for these FGIDs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0385 ARE CONDITIONS OF IMMUNE DYSREGULATION RISK FACTORS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS? FINDINGS FROM A RANDOM POPULATION-BASED STUDY


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**Introduction:** The prevalence of disorders of immune dysregulation is rising. [1] Inflammatory bowel disease and coeliac disease [2] as well as rheumatoid disorders [3] have been shown to be more common among patients with functional gastrointestinal disorders (FGIDs) including irritable bowel syndrome (IBS). Little is known however about whether other types of immune disorders are also associated with FGIDs in the community.
**Aims & Methods:** In a population-based study we aimed to determine whether disorders of immune dysregulation are risk factors for IBS and functional dyspepsia (FD). A total of 3576 people (mean age 58.5 years, age range 18–100 years and 47.6% males) randomly selected from the Australian population returned a mail survey (response rate = 43.6%). The survey contained self-reported questions on whether the participant had ever been told by a doctor that they had the following immune diseases including scleroderma, diabetes mellitus, rheumatoid arthritis, coeliac disease, ulcerative colitis (UC) and Crohn's disease (CD). IBS including constipation predominant (IBS-C) and diarrhoea predominant IBS (IBS-D) and FD were diagnosed according to modified Rome III criteria. Post infectious IBS (PI-IBS) was defined by the presence of gastroenteritis in the 3 months preceding the onset of symptoms. In a multivariate model these factors along with other health conditions, lifestyle (BMI, smoking, sleep problems, proton pump inhibitor usage), psychological disturbance and age and gender were evaluated.
**Results:** Among the general population 25.5%, and 14.6% met modified Rome III criteria for IBS and FD, respectively. As expected UC was significantly more common in people with IBS including IBS-D, with UC and CD remaining independent risk factors for IBS (OR = 4.46; 95%CI 2.11, 9.44, P = 0.001; OR = 3.62; 95%CI 1.12, 11.67, P = 0.03) and IBS-D (OR = 5.53; 95%CI 2.73, 11.21, P < 0.001; OR = 6.61, 95%CI 1.88, 23.23, P = 0.003) in the multivariate model respectively. Ulcerative colitis (OR = 3.01; 95%CI 1.53, 5.94, P = 0.001) and Coeliac disease (OR = 2.51; 95%CI 1.21, 5.19, P = 0.01) were also independent predictors of FD. Rheumatoid arthritis was significantly associated with IBS and PI-IBS but was not an independent risk factor for these conditions. Scleroderma and diabetes mellitus were not significantly associated with either IBS or FD (Table 1).

**Table 1:** Univariate associations of immune dysregulation disorders and IBS and FD.

| | IBS Yes n (%) vs. No n (%) CI (95%CI) P value | FD Yes n (%) vs. No n (%) CI (95%CI) P value |
|---|---|---|
| Scleroderma | 2 (0.2)<br>12 (0.5)<br>0.49 (0.11, 2.18)<br>P = 0.4 | 2 (0.4)<br>12 (0.4)<br>1.0 (0.22, 4.36)<br>P = 0.9 |
| Diabetes mellitus | 87 (9.8)<br>281 (10.8)<br>0.89 (0.69, 1.15)<br>P = 0.4 | 57 (11.1)<br>313 (10.5)<br>1.07 (0.79, 1.44)<br>P = 0.7 |
| Rheumatoid Arthritis | 74 (8.3)<br>162 (6.2)<br>1.37 (1.03, 1.82)<br>P = 0.03 | 44 (8.6)<br>191 (6.4)<br>1.38 (0.98, 1.94)<br>P = 0.07 |
| Ulcerative Colitis | 31 (3.5)<br>23 (0.9)<br>4.05 (2.35, 6.98)<br>P < 0.001 | 26 (3.5)<br>28 (0.9)<br>4.01 (2.34, 6.89)<br>P < 0.001 |
| Crohn's disease | 9 (1.0)<br>12 (0.5)<br>2.20 (0.93, 5.25)<br>P = 0.07 | 5 (0.1)<br>16 (0.5)<br>1.83 (0.67, 5.02)<br>P = 0.24 |
| Coeliac Disease | 14 (1.6)<br>34 (1.3)<br>1.21 (0.64, 2.56)<br>P = 0.6 | 16 (3.0)<br>33 (1.1)<br>2.89 (1.58, 5.29)<br>P = 0.001 |

**Conclusion:** We found evidence for an increased risk of some disorders of immune dysregulation including inflammatory bowel disease, rheumatoid arthritis and Coeliac disease and the FGIDs IBS and functional dyspepsia in the general population. Further research is needed to determine whether these conditions share a similar underlying pathophysiology or are due to other factors such as medication side effects.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0387 PERCEPTIONS OF PATIENTS WITH IRRITABLE BOWEL SYNDROME IN RELATION TO THE CARE RECEIVED IN THE PUBLIC HEALTH SYSTEM IN SPAIN


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**Introduction:** Irritable bowel syndrome (IBS) is a common disorder characterised by recurring abdominal pain and altered bowel movements. The pathophysiology of IBS is not fully understood, and there is no validated biological diagnostic marker. As a result, patients often feel frustrated by a lack of information and perceive a stigma associated with their symptoms. A strong healthcare provider (HCP)–patient relationship is associated with increased patient satisfaction and improved outcomes, and as such is central to the effective diagnosis and management of IBS.
**Aims & Methods:** The objective of this study was to identify potential barriers as perceived by patients with IBS in relation to the care they received in the public health system in Spain. This was a multicentre, cross-sectional observational

study. Patients (aged ≥ 18 years) who attended a private consultation with a gastroenterologist (GE) for constipation and abdominal discomfort, had no previous IBS diagnosis, and who met Rome III criteria for IBS without alarm symptoms, were included. Patients completed the IBS-Symptom Severity Score questionnaire, EuroQol five dimensions (EQ-5D) quality of life questionnaire, and the Irritable Bowel Syndrome Patient Experience questionnaire, which comprises questions relating to patient experiences with both their primary care physician (PCP) and their GE.

**Results:** A total of 707 patients completed the study; 81% were female and the mean age was 45.6 years. The majority of patients (87.1%) met the criteria for IBS with constipation (IBS-C), with 11.9% of patients having mixed or unclassified IBS. The median time elapsed since patients' first visit to a HCP for their symptoms was 2 years. The main reason patients reported visiting a private GE was to seek a second opinion (41.4%) or because they felt their public HCP had not resolved their condition (36.4%). Overall, most patients reported suffering moderately severe symptoms (68.9%). Patients reported frequently suffering from abdominal pain (90%) and abdominal distension (91.5%), and the average severity of these symptoms on a scale of 0–100 was 58.3 ± 18.3 for abdominal pain and 61.9 ± 17.9 for abdominal distension. EQ-5D survey results showed that 61.5% of IBS patients reported moderate or severe problems with pain/discomfort, and 41.9% reported mild or moderate problems with everyday activities. Patients reported that their current treatment was offering little (47%) or some (25.9%) improvement in symptoms. In general, patients' perceptions were more positive towards their GE than their PCP, with only 43.9% of patients satisfied with the care received by their PCP, compared with 62.8% for their GE (**Table**).

**Conclusion:** IBS symptoms impact patients' quality of life and many patients experience symptoms for several years before being formally diagnosed. Moreover, many IBS patients feel they are not listened to when seeing a HCP, especially in the case of primary care. These data in patients with IBS-C highlight the high unmet need for improved provider–patient communication in relation to IBS, in order to improve both diagnosis and patient outcomes.

**Disclosure of Interest:** X. Cortés Gil: Xavier Cortés Gil is an employee of Almirall.

All other authors have declared no conflicts of interest.

**Table:** Summary of selected questions from the Irritable Bowel Syndrome Patient Experience questionnaire.

| Question, % | Primary care physician | | Gastroenterologist | |
|---|---|---|---|---|
| | Yes | No | Yes | No |
| Do you feel that your provider listens to you and takes into account what you are saying when you speak? | 59.4 | 40.6 | 77.4 | 22.6 |
| Does your provider give you enough time in the consultation for you to be able to properly tell them what is wrong? | 30.5 | 69.5 | 53.5 | 46.5 |
| Does your provider give you written information about, for example, diet or other instructions to help you feel better and follow the treatment correctly? | 28.9 | 71.1 | 50.1 | 49.9 |
| Do you feel you are wasting your time when you attend the consultation with your provider? | 52.4 | 47.6 | 27.8 | 72.2 |
| Do you trust that your provider is knowledgeable about what is wrong with you and chooses the appropriate treatment? | 33.7 | 66.3 | 63.6 | 36.4 |
| In general, are you satisfied with the care you receive from the provider you normally see? | 43.9 | 56.1 | 62.8 | 37.2 |

## P0388 PROTON PUMP INHIBITORS INCREASE THE RISK FOR IRRITABLE BOWEL SYNDROME - A POPULATION-BASED STUDY

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**Introduction:** Proton pump inhibitors (PPIs) are widely prescribed in gastroenterology and general practice. Recent literature supports a change in the gut microbiome in patients on long term PPIs (1, 2). Irritable bowel syndrome (IBS) is a disease with unclear pathophysiology and risk factors although alterations in the microbiome have been implicated as a mechanism (3). Little is known about the link between PPI use and IBS, although a link with small intestinal bacterial overgrowth has been implicated (4).

**Aims & Methods:** In a population-based study we aimed to determine the prevalence of IBS in participants taking PPIs. A total of 3576 people (mean age 58.5 years, age range 18 to 100 years, 47.6% males) randomly selected from the Australian population returned a mail survey (response rate = 43.6%). IBS including constipation predominant and diarrhoea predominant IBS subtypes was diagnosed according to modified Rome III criteria. Post infectious IBS was defined by the presence of gastroenteritis in the 3 months preceding the onset of symptoms. The survey contained a self-reported question on whether the participant was taking PPIs.

**Results:** Amongst the general population, 25.5% met the ROME III criteria for IBS and 14.6% for functional dyspepsia (FD). A total of 631 (17.6%) subjects were taking PPIs. Of those on PPIs, 228 (36.3%) had IBS and on subtype analysis, 7.2% of people had IBS–constipation (IBS-C) and 8.8%, IBS-diarrhoea (IBS-D). Post-infectious IBS was present in only 4% of participants with IBS on PPIs. Also, 27.3% of patients on PPIs had FD as diagnosed by ROME III criteria, suggesting this was the most common indication for PPI use. In the multivariate analysis including a range of self-reported health conditions, demographic, lifestyle (smoking, BMI, sleep problems) and psychological distress, those on PPIs showed an odds ratio of 1.75 (95% CI 1.31–2.34, $p < 0.001$) for concurrent IBS and PPI use.

**Conclusion:** Based on a large population-based study, we confirm that the prevalence of IBS is higher in patients taking PPIs, in line with a previous report from the USA (4). This may be secondary to an alteration in the gut microbiome. The general notion that PPIs are harmless might not hold true and further research is needed to elucidate the complex relationship between acid suppression and gut health.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0389 ASSOCIATIONS BETWEEN HYDROGEN BREATH TEST AND SYMPTOM RESPONSES DURING A LACTULOSE NUTRIENT CHALLENGE IN IBS PATIENTS AND HEALTHY CONTROLS

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**Introduction:** Irritable Bowel Syndrome (IBS) is associated with increased symptom levels after a lactulose challenge test, compared to healthy controls (Le Nevé et al, *AJG* 2013), with psychological distress and co-morbid functional dyspepsia (FD) also being associated with symptom levels (Pohl & Van Oudenhove et al, *UEGW* 2015). However, it remains unknown whether hydrogen breath test responses and symptom responses to this test are associated.

**Aims & Methods:** 196 IBS patients (Rome III), 81 of which had co-morbid FD (43.6%), and 81 healthy volunteers (HV) consumed a 400-ml liquid breakfast (Nutridrink®) combined with 25 g of lactulose after an overnight fast. They completed visual analogue scales (0–20) assessing severity of five gastrointestinal (GI) symptoms (abdominal pain, bloating, nausea, gas, urgency) and digestive comfort before breakfast and every 15 minutes up to 240 minutes post-lactulose ingestion, and hourly for 240 more minutes after intake of a standardized lunch. Breath samples were collected and analysed at the same time points up to 240 minutes post-lactulose ingestion for hydrogen level measurement using a gas chromatograph. The relationship between peak hydrogen level (increase from baseline) and GI symptom levels over time was analyzed using linear mixed models, controlling for gender and anxiety, depression, or somatization.

**Results:** No significant main or interaction effects of delta peak hydrogen were found for bloating and urgency. For nausea, a significant main effect of delta

peak hydrogen was found ($p = 0.028$), driven by a positive association between hydrogen response and symptom level over the entire period of measurement. For gas, a significant delta peak hydrogen-by-time interaction effect was found ($p = 0.013$), driven by a positive association between hydrogen response and symptom level from 195 minutes post-lactulose ingestion on. For abdominal pain and digestive comfort, a group-by-time-by-delta peak hydrogen three-way interaction effect was found ($p = 0.003$ and $p = 0.059$, respectively), driven by a lack of association between hydrogen response and symptom levels in healthy controls, a main effect of delta peak hydrogen in IBS patients without FD, and a time-by-delta peak hydrogen interaction effect in IBS patients with FD (with the strongest relationship in the beginning of the measurement and after lunch). The effect of the psychosocial variable was significant for all symptoms, confirming earlier findings.

**Conclusion:** Increased hydrogen production during a lactulose-nutrient challenge test is associated with higher levels of nausea, gas, and abdominal pain, and lower levels of digestive comfort.

**Disclosure of Interest:** D. Pohl: Daniel Pohl has served as Consultant for Astra Zeneca, Allergan and Takeda and as Speaker for Allergan, Almirall, Astra Zeneca, Sucampo and Takeda.

H. Törnblom: Hans Törnblom has served as Consultant/Advisory Board member for Almirall, Danone and Shire.

B. Le Nevé: Boris Le Nevé is employed by Danone Research.

J. Tack: Jan Tack has served as Consultant/Speaker for: Abbott, Almirall, AlfaWasserman, AstraZeneca, Danone, Janssen, Menarini, Novartis, Nycomed, Ocera, Ono pharma, Shire, SK Life Sciences, Theravance, Tranzyme, Xenoport, Zeria Pharmaceuticals.

M. Simrén: Magnus Simrén has received grants from Danone, and Ferring Pharmaceuticals, and served as a Consultant/ Speaker for Albireo, Allergan, Almirall, Astra Zeneca, Danone, Glycom, Chr Hansen, Nestlé, Shire, Takeda and Tillots.

All other authors have declared no conflicts of interest.

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### P0390 MIXTURE-MODEL BASED SUBGROUPING OF PATIENTS WITH IBS

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**Introduction:** Irritable Bowel Syndrome (IBS) is a heterogeneous disorder with no clear pathophysiological explanations, and therapy options are sparse. Current subgroupings are based on bowel habits and do not consider other gastrointestinal, psychological or extraintestinal symptoms. Our aim was to evaluate a subgrouping strategy based on detailed symptom profiles.

**Aims & Methods:** A mixture model analysis (latent classes) was used to identify naturally occurring subgroups of IBS patients based on GI, extraintestinal and psychological traits. Traits included the 13 single-item scores from the IBS specific Gastrointestinal Symptom Rating Scale (GSRS-IBS) to account for a profile of GI symptoms, and the average stool consistency and frequency from a six-day stool diary. Psychological symptoms included anxiety and depression from the Hospital Anxiety and Depression scale and three subscores each from the Fatique Impact Score (FIS) and the Sense of Coherence questionnaire (SOC), respectively. Extraintestinal symptoms were drawn from the Patient Health Questionnaire. From these measures we derived two latent classification systems: The first based on all 13 gastrointestinal symptoms only, and a second where we added psychological and extraintestinal symptoms. Latent classes were then compared with respect to symptom profiles using analysis of variance and pair-wise comparisons.

**Results:** We analyzed 172 well-characterized patients with IBS (Rome III criteria, 69% female; mean age 33.7 (range: 18–60 years). Rome III based subgrouping showed 20 patients with IBS-C (11.6%), 42 with IBS-D (24.4%), 107 with IBS-M (62.2%) and 3 patients with IBS-U (1.7%). Our first classification based on 15 gastrointestinal symptoms (GIM) showed an optimal solution for three subgroups. These were characterized by symptom profiles of a) constipation, abdominal distention, incomplete bowel emptying ($n = 69$), b) diarrhea, urgency, pain ($n = 72$), c) less than average symptom severity ($n = 31$) (Figure 1). We then compared these groups regarding psychological and extraintestinal symptoms. Significantly higher anxiety levels could be attributed to the diarrhea-pain group. The low-symptom group showed significantly lower levels of psychological and extraintestinal symptoms and higher levels of SOC, as well as significantly lower scores for dizziness and fainting (Figure 2 and 3). A comparison of these three groups with the Rome III subgroups showed a high overlap for IBS-C and IBS-D with the constipation-abdominal distention and diarrhea-pain group, respectively, whereas IBS-M and IBS-U where quite evenly distributed between latent classes. All Rome subgroups showed overlap with the low symptom group (Table 1). The model based on a combination of all considered symptoms showed an optimal solution for two groups, characterized by a) high overall symptom burden, b) low overall symptom burden. A comparison with Rome subgroups exhibited no clear clustering.

**Conclusion:** This model-based subgrouping partly supports the distinction of subgroups based on bowel habits, but takes other gastrointestinal symptoms and severity into account and uses a symptom profile to characterize subgroups. The association of gastrointestinal, psychological and extraintestinal symptoms is generalized across a profile and not solely focused on a single construct. As a next step we will compare these latent classes regarding underlying pathophysiological mechanisms.

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### P0391 LABORATORY INVESTIGATIONS FOR PATIENTS MEETING DIAGNOSTIC CRITERIA FOR IRRITABLE BOWEL SYNDROME: ARE WE MEETING THE STANDARDS?

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**Introduction:** Alongside a thorough clinical assessment the UK National Institute for Clinical Effectiveness (NICE) clinical guideline 61 recommends that patients meeting diagnostic criteria for irritable bowel syndrome (IBS), as defined by the Rome III criteria, should undergo laboratory testing for inflammation (C-reactive peptide (CRP) and plasma viscosity (PV) or erythrocyte sedimentation rate (ESR)), full blood count (FBC) and antibody testing for coeliac disease to exclude non-organic pathology [1]. Faecal calprotectin is a reliable and cost effective adjuvant test to help differentiate between functional and inflammatory bowel disease (IBD) [2, 3].

**Aims & Methods:** Our aim was to assess local adherence to NICE guidelines on investigating patients who meet diagnostic criteria for IBS. As part of a wider study into the use of faecal calprotectin as a diagnostic tool within Gloucestershire Hospitals NHS Foundation Trust, UK, we interrogated clinic letters, endoscopy reports and pathology results for patients in whom a negative ($< 50$ mg/g faeces) or intermediate (50–150 mg/g faeces) faecal calprotectin level had been measured between September 2014 and September 2015. In patients diagnosed with IBS, we identified which of CRP, PV/ESR, FBC and antibody testing for coeliac disease had been done prior to or concurrent with faecal calprotectin measurement.

**Results:** Of the 148 patients (age range: 16–81, median age: 35; 72% female) who satisfied inclusion criteria, 63.5% ($n = 94$) had not undergone at least one of the recommended laboratory tests around the time of faecal calprotectin measurement. PV/ESR had not been checked in a majority (54.1%). Notably, 7.4% of patients had never had coeliac serology checked, 72.7% of whom presented with a change in bowel habit.

**Conclusion:** Although clear guidance exists for the investigation of patients meeting diagnostic criteria for IBS and use of faecal calprotectin as a diagnostic tool, insufficient essential accessory investigations are being completed. This risks conditions such as IBD, gastrointestinal cancer and coeliac disease being misdiagnosed as IBS with significant implications for delays in management and ongoing avoidable morbidity. We are reviewing measures to improve local adherence to NICE guidance, and call on other Trusts internationally to reflect on their own practice.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0392 MANAGEMENT OF IRRITABLE BOWEL SYNDROME IN A DISTRICT HOSPITAL

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**Introduction:** Irritable bowel syndrome (IBS) is a chronic, relapsing and often lifelong disorder. It is characterised by the presence of abdominal pain or discomfort, which may be associated with defaecation and/or accompanied by a change in bowel habit.

**Aims & Methods:** We compared the management of IBS with standards set up by NICE. Ensuring the correct management of IBS will improve the quality of life of the patients as well as being cost effective in term of avoiding unnecessary

investigations and admissions. Over a seven-month period, information was gathered retrospectively on 66 patients (18–90 year old) referred to the gastroenterology out patient clinic with a suspected diagnosis of Irritable Bowel syndrome.

**Results:** The management of those patients was assessed against NICE guidelines (NICE guidelines 61, 2008). include establishing a diagnosis; identification of 'red flags' (symptoms and/or features that may be caused by another condition that needs investigation); avoiding unnecessary investigations; providing lifestyle advice; drug and psychological interventions; and referral and follow-up. The results showed that most of the patients (85% -100%) were assessed and clinically examined for the ''red flag'' signs and symptoms like weight loss, anaemia, abdominal mass, rectal bleed, or family history of bowel or ovarian cancer. Majority of the patients (94%–100%) had the basic blood tests (Full blood count, ESR, CRP). However, only 34% were had antibody testing for coeliac disease. There was a clear insufficiency (45% -65%) in providing information about IBS explaining the importance of self-help in effectively managing their IBS including life style, diet, and physical activity. High percentage of patient with clinical diagnosis of Irritable bowel syndrome had unnecessary investigations like upper or lower endoscopy (76%) and abdominal ultrasound scan (48%).

**Conclusion:** The use of the national guidelines to make appropriate diagnosis and management for Irritable bowel syndrome can improves patients' quality of life and avoids exposing them to unnecessary tests like colonoscopy. The study showed that there is a general tendency to over investigate patient with suspected IBS despite the absence of the red flag signs and symptoms. Most of the patients did not have the appropriate information and advice regarding their disease management. National guidelines are helpful tools in management patients; however, to avoid missed diagnoses of serious disease, using the guidelines must be tailored to the specific clinical setting.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0393 PERFORMANCE EVALUATION OF DYSBIOSIS STATUS AS A TOOL FOR CLINICAL INVESTIGATION IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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**Introduction:** Probiotic treatments in patients with functional gastrointestinal disorders (FGID) show promising effects. Because of a lack of tests for routine diagnosis of dysbiosis as yet bacteriotherapy cannot be targeted.

**Aims & Methods:** A commercially available stool dysbiosis test (GA-map™ Dysbiosis Test[1]) was performed in patients with FGID to analyze individual microbiota and to define goups of patients according to their symptoms and microbiota profiles. The dysbiosis test is a 16 S rRNA DNA test that utilizes DNA probes in recognizing gut bacteria profiles for identification and characterization of dysbiosis. The study took place in 7 private gastroenterology praxes all over Germany and included 99 eligible outpatients. Age of the patients ranged from 16 to 84 years (median age 44) and sex ratio was 70% females. Informed, written consent was given by each patient.

**Results:** Stool testing was feasible and complete in all included patients. A dysbiosis index score (DI) consisting of 5 levels (1–2: non dysbiotic, 3–5 dysbiotic) was defined in 99 patients. According to the cut off of the dysbiosis test, 31 patients (31%) had no dysbiosis while the majority of patients (69%) were dysbiotic. Dysbiosis was mainly associated with augmented Ruminococcus gnavus, and Proteobacteria and diminished Faecalibacterium prausnitzii. Subgroups with elevated levels of dysbiosis could be identified such as FGID after travelers' diarrhea (82% dysbiosis, 9/11 patients), as compared to diarrhea predominant FGID (69%, 42/61 patients) with dysbiosis not different from the majority of patients, and a group of 13 low-grade inflammatory patients harboring severe dysbiosis. All subgroups showed different bacterial profiles.

**Conclusion:** The dysbiosis test available for clinical routine testing is able to identify dysbiosis in symptomatic patients with FGID in a daily routine setting. Accurate diagnosis of the microbiota offers the possibility of targeted bacteriotherapy.

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T. Lindahl: Employee of Genetic Analysis.
E. Ciemniejewska: Employee of Genetic Analysis.
C. Casén: Employee of Genetic Analysis.
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## P0394 NEGATIVE FAECAL CALPROTECTIN TESTING PROVIDES COST-EFFECTIVE DIAGNOSTIC REASSURANCE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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**Introduction:** The diagnosis of irritable bowel syndrome (IBS) requires careful exclusion of 'red flag' clinical features and blood abnormalities which may indicate an alternative organic diagnosis such as inflammatory bowel disease (IBD).[1] The chronic, recurrent nature of the symptoms of IBS may lead to diagnostic anxiety. Faecal calprotectin (FC) is a useful non-invasive test for intestinal inflammation that can distinguish IBS from IBD when specialist referral or further investigations are being considered.[2] Confident use of FC is likely to save costs by reducing referral and endoscopy burden.

**Aims & Methods:** This retrospective, observational study investigated the management of patients diagnosed with IBS following gastroenterologist review who had negative FC (<50 µg/g faeces) tested between September 2014 and September 2015 in Gloucestershire, UK. Electronic records were interrogated for clinical letters and the results of blood (full blood count, C-reactive peptide, erythrocyte sedimentation rate/plasma viscosity and coeliac serology), stool and endoscopic investigations. Red flag indicators were defined as per NICE clinical guideline 61.[1] The cost-saving implications of negative FC testing to confirm IBS were evaluated using estimated per person costs of an ELISA test and POCT CalDetect (£22.79), outpatient gastroenterology appointment (£164.00), colonoscopy (£577.68) and flexible-sigmoidoscopy (£351.00).[2, 3].

**Results:** During the study period 173 non-IBD patients (age range: 17–81 y, median: 35 y, 72% female) were referred for gastroenterologist review and had a negative FC test. There were no documented red flag clinical features nor significant abnormalities on blood testing in 30 patients diagnosed with IBS. 23% and 17% of these patients had undergone colonoscopy and flexible sigmoidoscopy respectively. No significant abnormalities were detected. The estimated cost-saving impact of a negative FC to confirm a diagnosis of IBS and limit unnecessary referral and endoscopy was £357.29 per person.

**Conclusion:** A negative FC may provide cost-effective diagnostic reassurance in patient with suspected IBS without red flag clinical features or blood abnormalities in whom specialist referral or endoscopy is considered. There is a need for FC testing to be made available to primary care physicians with robust pathways to support decision-making.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0395 PERFORMANCE OF A NOVEL CARE PATHWAR FOR FUNCTIONAL GASTROINTESTINAL DISORDERS: A PILOT STUDY-INTERIM RESULTS

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**Introduction:** Large numbers of referrals for specialist gastroenterology outpatient care result in long waiting lists and reduce or delay access to a diagnosis and effective management for referrals judged less ''urgent''. Many non-urgent referrals are for people with likely functional gastrointestinal disorders (FGID). Therefore, new models of care are needed to more efficiently transfer specialist-held expertise in FGIDs out to primary care practitioners.

**Aims & Methods:** This study aims to evaluate the performance of a non-specialist dependent algorithm-based approach to the diagnosis and management of FGID. Consecutive patients triaged to the 'routine waitlist' of an Australian public hospital Gastroenterology Department over 2 years, with non-specific GI symptoms (no alarms) were randomised to waitlist control or the algorithm (2:1). Algorithm patients were screened for organic disease with a standard questionnaire for alarms and a routine panel of blood/stool tests (full blood count, C-reactive protein, biochemistry, thyroid function tests, iron studies, coeliac serology, +/- *H. pylori* serology, +/- faecal calprotectin and elastase). In cases where patients had clinical alarms or abnormal tests, data were reviewed by a gastroenterologist (GE) and, if appropriate, prompt GE appointment offered. Those without screening concerns were classified according to Rome III criteria and received a letter which explained their FGID diagnosis and dietary/psychological management options. Waitlist control patients were not screened. All participants completed symptom severity, quality of life, workplace productivity and mental health surveys at baseline and 6 weeks.

**Results:** 90 algorithm patients (61% female, mean 42, [SD 14] y) and 21 control (75% female, mean 43, [SD 16] y) patients completed intake. Of the 90 patients screened with the algorithm 47 were diagnosed FGID, 34 warranted prompt GE review (diagnoses = 15 FGID, 2 IBD, 5 other, 12 pending), and 9 were excluded.

34 algorithm patients completed 6 weeks follow up and compared to controls, showed reduced GI catastrophizing cognitions [t (50) = -4.27, p < .001], anxiety [t (47) = -2.35, p = .023] and stress [t (47) = -2.41, p = .020] whilst GI symptom severity did not change [t (50) = −0.171, p = .865]. GI-specific anxiety was higher than controls at 6 weeks [t (50) = 2.46, p = .017), but unchanged from baseline [t (34) = 1.251, p = .215]. 33/34 patients had read the letter and only 1 rejected the diagnosis. Most patients found the letter useful (23/34): as it provided a diagnosis (n = 5), management options (n = 6) and reassurance (n = 7). Two felt the algorithm did not take their full situation into account (Table). Only 9/34 discussed the letter with their GP yet 23 proceeded with management options. Dietary management (14 diet only, 1 psychology only, 8 both, 11 neither) and self-help options (47% self-help only, 21% self-help/face-to-face) were preferred, with symptom improvement in 17 of the 34 respondents at 6 weeks, and the approach was acceptable to 19 of these. We postulate that the difference in GI-specific anxiety between control and algorithm group may be a side effect of monitoring, or a delay between cognition changes affecting GI-specific anxiety. However, the algorithm was able to reduce overall stress and anxiety by providing reassurance and management tools.

Patient Feedback on the Usefulness of the Diagnostic/Management Letter

| | |
|---|---|
| Useful | "It was good to know what was wrong with me and that there were options for managing it". Pt #3 |
| | "Stopped me worrying it was something serious". Pt #31 |
| | " It has help to reduce my stress level... I am able to manage my health problem better and is feeling much better" Pt #32 |
| Ambivalent | "Confirmed possible diagnosis. But would prefer to have a colonoscopy to double check all is ok" Pt #25 |
| | "I know it was meant to be reassuring that there is nothing sinister, but without definite proof I find it hard to relax" Pt #34 |
| Not Useful | "I did not find the letter and diagnosis useful, I felt that my case had not been thoroughly considered and that that I had many questions left unanswered". Pt #5 |
| | "No. All my problems were not included or asked about, fat malabsorption or floaty stool, lactose intolerance..." Pt #33 |

**Conclusion:** This novel FGID care pathway was effective at improving patient outcomes by providing a diagnosis, reassurance, and evidence-based management options without accessing face-to-face specialty care. Patient acceptability and buy-in was good, with the majority of respondents achieving symptomatic improvement and reduced stress and anxiety. Future research trialing the 'FGID Care Pathway' in either primary or tertiary care would be beneficial.
**Disclosure of Interest:** E.C. Linedale: Abbott's Pathology provided funding for the cost of routine stool tests used in this study.
All other authors have declared no conflicts of interest.

## P0396 REDUCTION OF SYMPTOMS AND BREATH H2 PRODUCTION IN A SUBGROUP OF PATIENTS WITH IRRITABLE BOWEL SYNDROME CHARACTERIZED BY DISTINCT GUT MICROBIOTA ACTIVITY: EFFECT OF A FERMENTED MILK PRODUCT CONTAINING BIFIDOBACTERIUM LACTIS CNCM I-2494

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**Introduction:** The aim of this exploratory study was to assess the effect of 14 days consumption of a fermented milk product with probiotics (FMPP) on gastrointestinal (GI) symptoms and exhaled $H_2$ and $CH_4$ during a combined nutrient and lactulose challenge test (Le Nevé et al, 2013) in patients with irritable bowel syndrome (IBS).
**Aims & Methods:** We screened 125 patients with IBS (Rome III) from a secondary/tertiary care center. The fasted subjects were served a test meal consisting of a 400 ml liquid breakfast (Nutridrink®, 1.5 kcal/ml) containing 25 g lactulose. The intensity of eight meal-related GI symptoms, the overall level of digestive comfort and the amount of exhaled $H_2$ and $CH_4$ were assessed before and during 4 h after meal intake. The lactulose challenge test was repeated on the same subjects after they had consumed 125 grams of FMPP (fermented milk product containing B. lactis CNCM I-2494) or a control product twice daily for 14 days in a double-blind, randomized, parallel design. Active fraction of the fecal microbiota derived from RNA was profiled using 16 S Miseq analysis targeting V3-V4 variables regions from fecal samples obtained before and after the intervention period. Measured endpoints were the intensity of eight meal-related GI symptoms and the amount of exhaled $H_2$ and $CH_4$.
**Results:** A total of 108 patients with IBS were randomized; 4 patients withdrew from each group. Analysis by intention to treat (ITT) did not show any statistically or clinically relevant difference between groups. However, a post-hoc analysis in patients stratified according to their baseline $H_2$ breath level demonstrated that the FMPP intervention significantly reduced mean $H_2$ breath level ($p = 0.01$) vs. control in high $H_2$ producers (baseline $H_2$ breath level $\geq 10$ ppm; n = 21 FMPP; n = 12 control), and tended to decrease some meal-related GI symptoms (gas, discomfort, $p = 0.09$) vs. control. Within the active microbial community, the ratio Prevotella/Bacteroides was significantly higher in high $H_2$ producers ($p < 0.05$), indicating a higher activity of Prevotella. The FMPP intervention tended to decrease the ratio Prevotella/Bacteroides vs. control in high $H_2$ producers ($p = 0.07$). No significant difference was found between high $H_2$ producers and low $H_2$ producers regarding baseline clinical parameters (IBS-SSS, HAD score, Rome III subtype).
**Conclusion:** We could not demonstrate an effect of FMPP containing B. lactis CNCM I-2494 on exhaled $H_2$ and $CH_4$ and GI symptoms in the whole IBS group. However, a subgroup of patients with high $H_2$ production and increased Prevotella/Bacteroides activity ratio at baseline appeared to respond more favorably, indicating that the degree of microbial activity in the gut may predict the symptomatic response to a FMPP intervention. Further investigations are required to confirm that subgrouping IBS patients using exhaled gas could open new opportunities in the management of IBS.
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All other authors have declared no conflicts of interest.

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## P0397 EFFICIENCY OF FMT IN CASES OF "TREATMENT-RESISTANT" IBS

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**Introduction:** Abnormal microbiota has crucial role in the pathogenesis and expression of the intestinal manifestations of IBS [1]. Gut microbiota is already accepted as a therapeutic target. Regarding high efficacy faecal microbiota transplantation (FMT) in refractory *C. difficile* infection, this procedure has also been proposed for the treatment of IBS, especially in "treatment resistant" cases [2].
**Aims & Methods:** The aim of our study is to evaluate the efficiency of FMT in treatment of "treatment resistant" IBS. We enrolled 12 patients (75% women; 6 IBS-D, 5 IBS-C, and 1 IBS-M, according to the Rome III criteria), with continuous GI symptoms after adequate lifestyle modification, antibiotic, pre- and probiotic and antipsychotic drugs treatment. FMT through colonoscopy with or without consecutive enemas was performed to all patients. Quantifying severity of GI symptoms (abdominal pain, bloating, flatus) for all patients was performed by using VAS. Bowel habits evaluation was performed by Bristol stool scale and frequency assessment. Quality of life estimated with SF-36.
**Results:** Abdominal pain resolution or significant improvement ($p \leq 0.01$) was reported in 3 (25%) and 6 (50%) patients; one patient (8.3%) reported no change in pain level. Statistical significant reduction in bloating and flatus level was achieved in 2 (16.7%) and 7 (58.3%) patient, respectively. All IBS-D and IBS-M patients reported normalization of stool frequency and consistency, for all IBS-C patients was observed significant ($p \leq 0.01$) reduction in frequency of laxatives using; stool consistency was changed in 3 (60%) patients. Straining and incomplete defecation reported by 5 (41.6%) and 2 (16.6%) patients before FMT, were not observed after procedure. Quality of life was also improved in 11 (91.6%) of patient. Complete symptoms resolution or significant improvement was observed in 4 (33.3%) and 7 (58.3%) patients respectively. Adverse effects (temporary increasing in bloating intensity) was reported in 2 (16.7%) patients.
**Conclusion:** Significant rate of clinical improvement in of patient with refractory IBS symptoms after FMT and less number of adverse effects as temporary increasing in bloating intensity substantiates the possibility of its use as a therapeutic modality in such circumstances. Future studies are needed to accurate investigation of possibly adverse effects and long-term outcomes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0398 EFFICACY AND SAFETY OF LINACLOTIDE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: RESULTS FROM A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL IN CHINA AND OTHER REGIONS

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**Introduction:** Linaclotide (LIN) is a guanylate cyclase-C agonist approved for the treatment of irritable bowel syndrome with constipation (IBS-C) in adults in the US, EU, Switzerland, Canada, Mexico, and Hong Kong (290 -μg dose). There is a need in China for therapy that is well tolerated and effective in treating both bowel and abdominal symptoms of IBS-C.

**Aims & Methods:** To evaluate the efficacy and safety of LIN in patients with IBS-C in China and other regions. This Phase 3, double-blind trial randomized IBS-C patients to once-daily oral LIN 290 $\mu$g or placebo (PBO). Eligible patients met Rome III criteria for IBS and, during a 2-week pretreatment period, had an average of $\leq$5 spontaneous bowel movements (SBMs)/week and $<$3 complete SBMs (CSBMs)/week, and reported abdominal pain $\geq$2 days/week with average abdominal pain score $\geq$3.0 (11-point numerical rating scale; 0 = none, 10 = very severe). Patients reported bowel habits (SBMs, CSBMs, stool consistency, and straining) and abdominal symptoms (bloating, discomfort, and pain) daily throughout the pretreatment and 12-week treatment periods. Co-primary and secondary endpoints were tested using a predefined 3-step serial gatekeeping multiple comparisons procedure (MCP). Adverse events (AEs) were monitored.

**Results:** The intent-to-treat (ITT) population included 839 patients (mean age = 41 years; 82% female; 81% Asian). The trial met all primary and secondary endpoints under the MCP (see Table). Responder criteria were met by 60.0% of LIN patients vs. 48.8% of PBO patients for $\geq$30% decrease in abdominal pain or discomfort for $\geq$6 of 12 weeks (P = 0.0010), and by 31.7% of LIN patients vs. 15.4% of PBO patients for IBS degree of relief score $\leq$2 (considerably or completely relieved) for $\geq$6 of 12 weeks ($P < 0.0001$) (co-primary endpoints). Higher weekly responder rates among LIN vs. PBO patients were seen within the first 2 weeks and sustained over 12 weeks of treatment for abdominal pain/discomfort ($P < 0.05$ at weeks 2–12) and IBS degree of relief ($P < 0.05$ at all weeks 1–12). LIN showed significant improvements vs. PBO in all secondary endpoints: 12-week change from baseline in CSBM and SBM frequency, stool consistency, straining, abdominal pain, abdominal discomfort, and abdominal bloating (all $P < 0.0001$). Diarrhea, the most common AE, was reported in 9.4% of LIN patients and 1.2% of PBO patients. Discontinuation rates due to diarrhea were low (0.7% LIN, 0.2% PBO).

**Table:** Primary and Secondary Endpoint Results (ITT Population).

| | PBO (N = 422) | LIN (N = 417) | P value[d] |
|---|---|---|---|
| **Co-primary Endpoints (% Responders)[a]** | | | |
| $\geq$30% decrease in abdominal pain or discomfort, with neither score worsening from baseline, for $\geq$6/12 weeks | 48.8 | 60.0 | 0.0010 |
| IBS degree of relief score $\leq$2 for $\geq$6/12 weeks[b] | 15.4 | 31.7 | $<$0.0001 |
| **Secondary Endpoints (LS Mean Change from Baseline)[c]** | | | |
| CSBMs/week | 1.0 | 1.9 | $<$0.0001 |
| SBMs/week | 1.5 | 3.0 | $<$0.0001 |
| Stool consistency (7-point BSFS) | 0.8 | 1.5 | $<$0.0001 |
| Straining (5-point ordinal scale) | −0.7 | −1.0 | $<$0.0001 |
| Abdominal bloating (11-point NRS) | −0.9 | −1.5 | $<$0.0001 |
| Abdominal pain (11-point NRS) | −1.1 | −1.6 | $<$0.0001 |
| Abdominal discomfort (11-point NRS) | −1.0 | −1.5 | $<$0.0001 |

BSFS= Bristol Stool Form Scale; CSBM = complete SBM; ITT = intent-to-treat; LS = least squares; NRS = numerical rating scale; SBM = spontaneous bowel movement.

[a]P values based on a comparison of LIN vs. PBO using a Cochran-Mantel-Haenszel test controlling for geographic region.

[b]IBS degree of relief score $\leq$2 (7-point balanced ordinal scale) corresponds to a response of ''Considerably relieved'' or ''Completely relieved''.

[c]P values based on a comparison of LIN vs. PBO using an analysis of covariance model with treatment group and geographic region as factors and baseline value as covariate.

[d]All P values met the criteria for statistical significance under the MCP.

**Conclusion:** These results demonstrate that LIN improves IBS-C symptoms in a predominantly Chinese IBS-C population; results support earlier trials and expand on previous results. Study sponsored by AstraZeneca AB and Ironwood Pharmaceuticals, Inc.

**Disclosure of Interest:** D.S. Reasner: David S. Reasner is an employee of Ironwood Pharmaceuticals and owns stock/stock options in Ironwood Pharmaceuticals.
J.M. Johnston: Jeffrey M. Johnston was an employee of Ironwood Pharmaceuticals and owns stock/stock options in Ironwood Pharmaceuticals.
P. Zeng: Peter Zeng is an employee of AstraZeneca and owns stock/stock options in AstraZeneca.
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All other authors have declared no conflicts of interest.

## P0399 UK CLINICAL EXPERIENCE AT 12 WEEKS WITH LINACLOTIDE FOR IRRITABLE BOWEL SYNDROME WITH CONSTIPATION

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**Introduction:** Linaclotide, a guanylate cyclase-C agonist, has been shown in clinical trials to relieve constipation and improve abdominal pain and discomfort in patients with irritable bowel syndrome with constipation (IBS-C), but there are limited UK-specific 'real world' data to support this.

**Aims & Methods:** The aim of the present study was to describe 'real world' clinical experience of linaclotide treatment in the UK. A multi-centre, observational, uncontrolled, prospective 52-week study is ongoing in 8 specialist gastroenterology services in England and Scotland, with the primary objective to describe the change from baseline in IBS-Symptom Severity Scale (IBS-SSS) score at 12 weeks after linaclotide initiation. Consenting patients aged $\geq$18 years initiated on linaclotide for IBS-C as part of usual clinical care were recruited. Data on patient demographic and clinical characteristics, concomitant medication (any concomitant laxative use was based only on clinicians' routine advice and/or patients' personal choice), patient reported outcomes (including IBS-SSS) and adverse events (AEs) are being collected. Here we report analysis of real world clinical experience at 12 weeks following linaclotide initiation.

**Results:** 202 patients were evaluated (185 female [92%]). Patient baseline characteristics were as follows: median age 44.9 (range: 18–77) years; median time since IBS-C diagnosis 2.6 months (range: 0–68 years); 84 (42%) patients reported laxative use at baseline. Mean baseline IBS-SSS score overall was 339 (standard deviation [SD]: 92; n = 192); 128 (67%) patients had IBS-C classified as severe (scores $\geq$ 300), 54 (28%) moderate (175 $<$ 300), 9 (5%) mild (75 $<$ 175) and 1 (0.5%) in remission ($<$75). At 12 weeks, mean IBS-SSS score was 266 (SD: 119; n = 123); 50 (41%) patients had IBS-C classified as severe, 42 (34%) moderate, 22 (18%) mild, 9 (7%) in remission. There was a significant decrease in IBS-SSS scores between initiation of linaclotide treatment and the 12-week observation, with a mean decrease of 59.4 (SD: 98) points ($P < 0.001$; n = 120 patients with paired data); 67 (56%) of these patients reported responding to treatment (i.e. reduction of $\geq$50 points, OR score fell below 150 [for patients with baseline score $\geq$150]). Linaclotide treatment 12-week follow-up questionnaires were returned by 154 (76%) patients; of these, 87 (56%) remained on linaclotide (defined as $\geq$4 days treatment in last week) at 12 weeks. 67/154 patients (44%) discontinued linaclotide by 12 weeks; 44/154 (29%) cited unacceptable tolerability, mostly diarrhoea (29/154 [19%]; 15/29 [52%] were taking laxatives at baseline). Median (range) time to discontinuation for diarrhoea-related and unrelated reasons: 3.3 (0.1–11.6) and 5.1 (0.1–12.0) weeks, respectively. Overall, 127 AEs possibly related to linaclotide were reported in 74 patients (37%), with diarrhoea (n = 44 [22%]), abdominal pain/cramps (n = 19 [9%]) and inefficacy (n = 13 [6%]) being most common (see Table). AEs were reported in 41/84 patients taking laxatives at baseline (49%) and in 33/118 patients not taking laxatives at baseline (28%); there was a significant association between taking laxatives at baseline and the emergence of diarrhoea on treatment, with a higher proportion of patients experiencing diarrhoea among those taking laxatives (31% versus 15%, $P = 0.008$; see Table).

**Table:** Most common adverse events reported in patients treated with linaclotide according to baseline laxative use.

| Patients with AEs reported | No laxatives at baseline (n = 118) | Laxatives at baseline (n = 84) | Overall (n = 202) |
|---|---|---|---|
| **Diarrhoea**, n (%) | 18 (15%) | 26 (31%)** | 44 (22%) |
| **Abdominal cramps/pain**, n (%) | 8 (7%) | 11 (13%) | 19 (9%) |
| **Drug ineffective**, n (%) | 8 (7%) | 5 (6%) | 13 (6%) |

**Chi-square test $P = 0.008$.

**Conclusion:** Linaclotide significantly reduced mean IBS-SSS score at 12 weeks. Linaclotide was reasonably well tolerated; diarrhoea was the most commonly reported AE, consistent with clinical trial data and mechanism of action of linaclotide, and was more common in patients reporting laxative use at baseline compared to those not on baseline laxatives.
**Disclosure of Interest:** A. Emmanuel: AE: served on advisory boards for Almirall.
S. McLain-Smith: SM-S: commissioned by Almirall to provide research design, conduct analysis and scientific editorial services.
M. Rance: MR: an employee of Allergan UK Limited.
A. Agrawal: AA: received speaker fees from Almirall.
P.B. Allen: PB: received speaker fees from Almirall.
M. Eugenicos: ME: served on advisory committee for Almirall.
A.D. Farmer: AF: received speaker fees from Almirall.
Y. Yiannakou: YY: received educational grant and speaker fees from Almirall.
All other authors have declared no conflicts of interest.

## P0400 POSITIVE EFFECTS FIVE YEARS AFTER A STRUCTURED PATIENT EDUCATION (IBS SCHOOL) FOR PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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**Introduction:** Treatment options for patients with IBS are limited. Information and reassurance are suggested to be important components in the management of patients with IBS. Patient education has previously been demonstrated to improve symptoms, health-related quality of life and knowledge about IBS at six and twelve months follow-up. (Ringström et al. Eur J Gastroenterol Hepatol. 2010 & 2012) but no long-term follow-up studies are available.
**Aims & Methods:** The aim was to evaluate long-term effects annually over five years after participation in an IBS school. We included 158 patients (mean age 38 (18–68) years; 135 females) with IBS according to the Rome II criteria, who had participated in the patient education, consisting of six two-hour sessions, once per week with approximately ten patients per group. Five different health care professionals were responsible for one session each. The patients completed questionnaires at baseline and thereafter annually during five years to evaluate the perceived knowledge of IBS, GI symptoms (IBS Severity Scoring System, IBS-SSS), GI-specific anxiety (Visceral Sensitivity Index, VSI), psychological symptoms (Hospital Anxiety and Depression scale, HAD) and health-related quality of life (Short Form-36, SF-36).
**Results:** The patients experienced increased knowledge of IBS ($74 \pm 12$ vs. $44 \pm 23$ (mean $\pm$ SD); $p < 0.001$), and were more satisfied with that knowledge (VAS, $69 \pm 21$ vs. $30 \pm 23$; $p < 0.001$), reduced GI symptoms (IBS-SSS, $263 \pm 103$ vs. $304 \pm 97$; $p < 0.001$), reduced GI-specific anxiety (VSI, $30 \pm 17$ vs. $38 \pm 17$; $p < 0.001$), reduced general anxiety (HAD anxiety, $6.9 \pm 4.5$ vs. $8.0 \pm 4.5$; $p < 0.001$) and improved health-related quality of life (SF-36 Mental Component Score, $39 \pm 14$ vs. $36 \pm 12$; $p < 0.001$) one year after the IBS school compared to baseline. These results were maintained throughout the five-year follow-up period. Patients who completed questionnaires at $\geq 3$ time points during the five-year follow-up tended to be more anxious, report better physical health-related quality of life and to be older compared to those who responded $\leq$ twice; otherwise, there were no significant differences between these two groups.
**Conclusion:** A structured patient education for IBS patients improves knowledge about IBS, reduces GI and psychological symptoms, and improves health-related quality of life. These positive effects are sustained for at least five years after participation in the IBS School. Therefore, this seems to be an important tool in the management of patients with IBS.
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M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/ Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall.
All other authors have declared no conflicts of interest.

## P0401 CORRELATION BETWEEN FOOD INTAKE AND SYMPTOM SEVERITY IN IBS

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**Introduction:** Food consumption and diet are central issues that concerns patients with irritable bowel syndrome (IBS), and they frequently report associations between food ingestion and onset or worsening of gastrointestinal (GI) symptoms. The current understanding about the association between the intake of certain nutrients, food items and/or food groups, and the GI symptom pattern is poor.
**Aims & Methods:** The aims of this study were to determine the intake of energy and nutrients, as well as FODMAPs (Fermentable Oligo-, Di, Monosaccharides and Polyols) in patients with IBS, and to study the association between food and nutrient intake and the severity of GI symptoms. We included 116 patients who fulfilled the Rome III criteria for IBS (mean age 34 (18–60) years; 74% females). They completed a 4-day food diary, in which the quantities consumed were entered in grams or household measures. The intake of nutrients, including FODMAPs, as well as 14 different food groups, was calculated by using a dedicated software. The IBS symptom severity was assessed with the IBS severity scoring scale (IBS-SSS; range 0–500).
**Results:** The mean daily intake of energy was $2134 \pm 591$ kcal (mean $\pm$ SD); 37.6% of the energy came from fat, 16.3% and 41.2% from protein and carbohydrates respectively. The total intake of FODMAPs was $17.8 \pm 16.7$ g, of which 72.0% was lactose, 14.9% fructans, 6.3% polyols, 3.4% fructose in exess of glucose and 3.4% galacto-oligosaccharides.
According to IBS-SSS, the majority of patients reported moderate to severe IBS symptoms. The IBS symptom severity was negatively correlated with the total intake of energy ($r = -0.25$, $p = 0.007$), carbohydrates ($r = -0.24$, $p = 0.010$), vegetables ($r = -0.219$, $p = 0.019$), alcohol ($r = -0.218$, $p = 0.019$), fiber ($r = -0.239$, $p = 0.010$) and cereals ($r = -0.203$, $p = 0.029$), However, we could not show any significant correlations between the severity of IBS symptoms and intake of FODMAPs (total or FODMAP components), fat or protein, or other food groups.
**Conclusion:** In this study we demonstrate associations between the severity of IBS symptoms and intake of certain nutrients and food groups. The negative associations could potentially indicate dietary adjustments made by the patients to cope with symptoms. A relatively low intake of FODMAPs compared with other populations could also implicate that patients have restricted intake of FODMAPs to reduce symptom severity.
**Disclosure of Interest:** B. Le Nevé: Danone Nutricia Research employee.
B. Holmes: Danone Nutricia Research employee.
H. Törnblom: Consultant/Advisory Board member for Almirall, Danone and Shire.
M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/ Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall.
All other authors have declared no conflicts of interest.

## P0402 USE OF LIFESTYLE INTERVENTIONS TO TREAT BOWEL AND/OR ABDOMINAL SYMPTOMS AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION (IBS-C) AND CHRONIC IDIOPATHIC CONSTIPATION (CIC): RESULTS FROM THE CONTOR STUDY

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**Introduction:** Most guidelines universally recommend the use of lifestyle interventions, such as increased dietary fiber, for the treatment of irritable bowel syndrome (IBS). This analysis examines the use of lifestyle interventions (e.g., diet, exercise) to treat bowel and/or abdominal symptoms among IBS-C/CIC patients participating in the Chronic **Con**stipation and IBS-C **T**reatment and **O**utcomes **R**eal-world Research Platform (CONTOR).
**Aims & Methods:** Fully insured patients $\geq$18 years old were identified from a large, geographically diverse US health plan based on claims from December 2012 through June 2015. Identification criteria included: $\geq$1 medical claim with a diagnosis of constipation (ICD-9-CM 564.0 x), IBS (ICD-9-CM 564.1 x), or abdominal pain (ICD-9-CM 789.0 x) plus $\geq$1 pharmacy claim for a stool softener/laxative; or $\geq$1 pharmacy claim for linaclotide or lubiprostone. Study participants completed a self-administered survey that included an assessment of prescription and over-the-counter medication use and lifestyle interventions ever used to treat their bowel and/or abdominal symptoms. Respondents were stratified by patient-reported current (last 7 days) medication use, including linaclotide, other prescription medications, and over-the-counter therapies.
**Results:** Of 18, 590 patients invited to participate, 2, 052 eligible patients responded and are included in this analysis. Respondents were predominately female (94%); mean age (SD) was 47 (12) years. Nearly all respondents reported experiencing bowel/abdominal symptoms for $\geq$2 years (92%), with nearly half (44%) experiencing symptoms for over 10 years. Almost all respondents (93%) reported using diet and/or other lifestyle interventions to treat their bowel/abdominal symptoms, with nearly 85% of respondents within each subgroup reporting use of dietary changes. A majority (93%) of respondents who reported using diet and/or exercise to treat their symptoms reported current medication use (within the last 7 days). Among current linaclotide users, more than two-thirds reported using both diet and exercise to treat their symptoms (Table). About half (53%) of all respondents reported using at least 2 lifestyle interventions to treat their bowel/abdominal symptoms (diet and exercise were the most common combination); 14% reported using 3 or more lifestyle interventions (diet, exercise, other). Less than 10% of respondents reported using no lifestyle interventions.
**Conclusion:** The majority of IBS-C/CIC patients have utilized both medication and lifestyle interventions to treat their bowel/abdominal symptoms, suggesting diet/exercise alone may not be sufficient to manage the symptoms of IBS-C and CIC.
**Disclosure of Interest:** J.L. Abel: Employee, stock holder and stock options from Allergan, plc.

**Abstract No: P0402**

**Table:** Patients using Lifestyle Interventions to Treat Bowel/Abdominal Symptoms by Current Medication Use[1]

| Lifestyle Changes, n (%) | Total (N = 2,052) | Linaclotide (N = 381) | Prescription Medications other than Linaclotide (N = 471) | Over-the-counter Medications Only (N = 715) | No Current Medication (N = 485) |
|---|---|---|---|---|---|
| Diet and Exercise | 1,290 (64) | 264 (69) | 270 (58) | 468 (66) | 288 (60) |
| Diet Only | 466 (23) | 58 (15) | 134 (29) | 162 (23) | 112 (23) |
| Exercise Only | 113 (6) | 27 (7) | 25 (5) | 41 (6) | 20 (4) |
| Other (includes acupuncture & other) | 29 (1) | 5 (1) | 7 (1) | 4 (1) | 13 (3) |
| None[2] | 136 (7) | 26 (7) | 33 (7) | 33 (5) | 44 (9) |

[1]Medication subgroups based on patient-reported current (last 7 days)

medication use. Patients with prescription and OTC medication use were included in the prescription medication analytic subgroups (Linaclotide and Other Prescription).

[2]18 patients did not select a response and are recorded as missing

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## P0403 EFFECTS OF FOOD ENRICHED WITH DIETARY FIBER IN WOMEN WITH CONSTIPATION-PREDOMINANT IRRITABLE BOWEL SYNDROME

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**Introduction:** Benefits of increased fiber intake for improvement of bowel function is well accepted, however most often average fiber intake is less than half of recommended amount.

**Aims & Methods:** The aim of the study was to supplement the dietary fiber intake up to recommended amount using interventions with less rough changes of food related behavior and investigate its effects on the bowel function, general well-being and compliance of patients with constipation-predominant irritable bowel syndrome (IRS-C). In total 100 healthy women, without any clinical signs of gastrointestinal disorders and 98 women who met Rome III criteria for IBS-C were enrolled in the dietary fiber intake assessment survey. There was no significant difference in average age among the groups ($33.7 \pm 16.7$ years and $39.2 \pm 12.3$ years, $p > 0.1$ respectively). After completion of the survey the women with IBS-C were assigned to daily intake of wheat bran-enriched bread (9.5 g dietary fiber per 100 g) and muesli (22.42 g dietary fiber per 100 g). Before, on the seventh day and on the end of two weeks of observation patients completed adopted questionnaire for assessment of bowel function and general well-being. The amount of added dietary fiber was $21.32 \pm 4.9$ g/daily. It made up average 40 g/daily intake of dietary fiber in women with IBS-C - excessive amount recommended for patients with constipation.

**Results:** The dietary fiber intake was significantly lower in the group of women with IBS-C ($18.7 \pm 4.9$ g) compared with healthy population ($27.8 \pm 5.55$ g, $p = 0.0022$), however the difference in consumption of carbohydrates between the groups was not considerable ($254.2 \pm 88.6$ g and $216.3 \pm 60.7$ g, $p = 0.17$ respectively). After 14 days the bowel movement increased significantly from $0.27 \pm 0.07$ up to $1.54 \pm 0.55$ times daily ($p < 0.0001$). 82 patients from initially enrolled 98 continuously received dietary fiber rich food during 14 days of observation, consequently the compliance rate was 83.7%. Before supplement of dietary fiber stool type was hard to pass in 70 from 82 cases (85.4%). After two weeks of eating of dietary fiber added food the stool was of normal consistency (Bristol scale level 3 and 4) in 76 cases (91.7%, $p < 0.0001$ respectively). Statistically significant improvement was observed in abdominal pain, the score decreased from baseline $0.75 \pm 0.11$ to $0.07 \pm 0.05$ points ($p = 0.0026$). The score relevant for difficulty of defecation decreased from $1.57 \pm 0.18$ up to $0.11 \pm 0.08$ points ($p < 0.0001$), the sensation of incomplete evacuation was decreased from baseline $1.96 \pm 0.13$ to $0.14 \pm 0.11$ points ($p < 0.0001$). Analyses showed significant decrease of alertness related to digestive feelings after continuous consumption of dietary fiber (from $1.04 \pm 0.31$ up to $0.18 \pm 0.07$ points, $p < 0.0001$).

**Conclusion:** Supplementation of dietary fiber with broadly used food products allows avoiding the changes of food-related habits and have a high compliance, also such intervention improves the bowel function and decreases alertness related to digestive feelings.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0404 SEVERE ACUTE ISCHEMIC COLITIS: WHAT IS THE PLACE OF ENDOSCOPY IN THE MANAGEMENT STRATEGY? A LARGE RETROSPECTIVE FRENCH STUDY

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**Introduction:** Ischemic colitis (IC) is the most common gastrointestinal vascular disease and could be potentially lethal. Clinic (shock), biology, CT scan and/or lower GI endoscopy are usually used to appreciate the severity. However, there is no consensus regarding this evaluation and it is challenging to choose between surgical or conservative treatment. To date, no studies have evaluated the prognosis of IC according to the endoscopic stages. Consequently, we propose this study to determine outcomes of patients depending on endoscopic findings, and the impact of endoscopy on the therapeutic decision.

**Aims & Methods:** This is a retrospective study conducted in a tertiary center, in North Hospital, Marseille, France. All the files of patients who had lower GI endoscopy for suspected ischemic colitis were reviewed in our database. Patients with confirmed severe ischemic colitis were kept for analysis. The following data were collected: age, Charlson comorbidity score, vascular disease, etiology including aortic surgery, clinical symptoms, organ failures, signs of severity in CT scan (effusion, enhancing defect or perforation), endoscopic stage of Favier, surgery and findings, death. The risk factors for colectomy and death were analyzed, and the correlation between endoscopic grade and outcomes was calculated. A p-value $< 0.05$ determined as statistically significant.

**Results:** Between 2006 and 2015, 118 patients were identified and 71 patients were finally included. They were 48 men (68%), and the mean age was $71 \pm 13$ years old. The mean Charlson score was $5.1 \pm 2.2$. The most common trigger factor for IC was surgery ($n = 34$; 48%), and especially aortic surgery ($n = 26$). Hemodynamic failure was present in 29 (41%) patients at the time of endoscopy. A CT scan was performed in 48 (68%) patients and identified a sign of severity in 18 (38%) patients. Twenty-nine (41%) patients underwent surgery, and twenty-four (34%) patients died, all being hemodynamically instable, except one. The endoscopic grades (100% of patients) were: 15 grade 1 (21%), 32 grade 2 (45%) and 24 grade 3 (34%). Regarding the patients with grade 3: 12 (55%) had hemodynamic instability, 14 had severity signs at CT scan, 15 (68%) underwent surgery and 12 (55%) died. Among the patients with grade 2: 10 (32%) had hemodynamic instability, 9 (29%) had signs of severity in CT scan, 10 (32%) underwent surgery and 9 (29%) died. Among the patients with grade 1: 7 (46%) were in shock, 4 (27%) underwent surgery, 2 had a sign of severity in CT scan and 3 (20%) died. A mismatch between mucosa (aspect of necrosis) and serous (normal aspect) was noted in 13 patients (46%), 6 had a colonic resection (4 deaths among these patients). The surgical decision was made on hemodynamic status in 62% of cases ($n = 18$), endoscopic grade in 10% ($n = 3$), the CT scan severity in 14% ($n = 4$) and other in 14% ($n = 4$). Risk factors for colectomy identified in univariate analysis were: aortic aneurysm surgery, hemodynamic failure, no colic enhancement in CT scan and endoscopic grade 3. Risk factors for mortality in univariate analysis were: hemodynamic failure, endoscopic grade 3, aortic aneurysm surgery, no colic enhancement in CT scan and Charlson score $> 5$. The Pearson correlation test showed a correlation of hemodynamic status with death and colectomy ($p < 0.01$). The endoscopic grade 3 was also correlated with colectomy and death ($p < 0.05$) but not with hemodynamic status.

**Conclusion:** This study suggested that endoscopy impacted on the decision to operate in situation of IC in only 10% of cases. However, colectomy and mortality were more frequent in patients with grade 3 endoscopic. Hemodynamic instability was the most frequent indication of colectomy in patients with ischemic colitis. A mismatch between mucosa and serous was present in 50% of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0405 COLON ISCHEMIA SEVERITY SCALE: EVALUATION AND DETERMINATION OF ADDITIONAL SEVERITY MARKERS

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**Introduction:** Recent American College Of Gastroenterology guidelines (2015)[1] proposed to redefine Colon Ischemia (CI) severity stratification into mild, moderate and severe disease in order to guide treatment. This classification assumes special importance in severe disease according to its high morbidity and mortality.
**Aims & Methods:** We aimed to evaluate the clinical evolution of patients hospitalized with CI diagnosis, taking into account the disease severity, and determine risk factors for severe disease classification. This is a retrospective study of all patients with definite diagnosis of CI according to Brandt criteria, from January 2010 to December 2015. We stratified patients according to the proposed classification and evaluated their evolution and prognosis. Additional clinical, histological, endoscopic and imagiologic features and its relation with the classification were considered.
**Results:** We selected 207 patients (72.9% female; mean age $72.3 \pm 13.0$ years), 21.7% (n = 45) with mild CI, 60.9% (n = 126) moderate and 17.4% (n = 36) severe. Patients with growing severity grade, mild, moderate and severe, had longer hospitalizations (4.8 vs. 6.6 vs. 11.1 days; $p < 0.001$), more surgery requirement (0% vs. 0% vs. 5.6%; $p = 0.008$) and recurrence rate (4.4 vs. 11.0 vs. 19.4%; $p = 0.036$), respectively. Mortality rate was similar between groups ($p = 0.270$). On univariate analysis, age, disease extension, disease in the rectum, non-description of erosions by the endoscopist, identification of bleeding, purulent material or necrotic cells on histologic analysis and the presence of occlusive vascular disease on computed tomography were associated with severe disease classification; $p < 0.05$. On multivariate analysis, independent features associated with severe disease classification were disease extension ($p = 0.005$; OR 1.14) and necrotic cells identification (0.047; OR 8.91); $R^2 = 0.68$.
**Conclusion:** The proposed classification properly stratifies CI patients regarding their clinical evolution and prognosis. Disease extension and necrotic cells identification in the histology are independent risk factors for severe disease classification.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0406 BILATERAL DIVERTICULOSIS IS AN INDIPENDENT RISK FACTOR FOR DIVERTICULAR BLEEDING: AN INTERIM ANALYSIS OF ONGOING STUDY

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**Introduction:** The natural history and pathogenesis of diverticular bleeding in Western population remains unclear. In Eastern population, the prevalence of right-side diverticulosis is higher than in Western one, and some Authors identified bilateral diverticulosis as a risk factor for bleeding in Eastern population.
**Aims & Methods:** The aim of this study was to evaluate whether right-side location of diverticular disease is a risk factor for bleeding also in Western world. We performed an interim analysis of a prospectively collected database; we analysed all patients admitted to Our Institution for acute diverticulitis and diverticular bleeding from January 2013 to December 2014. For each patient, age, gender, clinical presentation, concomitant medication, presence of divertula and their localization in the colon were recorded. All patient underwent computed tomography or colonoscopy during hospitalization, on the basis of clinical presentation. Patients who did not undergo endoscopic evaluation during the hospitalization, underwent complete colonoscopy or computed tomography colonoscopy within 3 months. Medacalc software was performed for statistical analysis.
**Results:** 144 patients (70 male, 48.3%; $77.4 \pm 14.0$ years-old) were prospecively enrolled. 85 patients (59.0%) were hospitalized for uncomplicated/complicated acute diverticulitis; 59 (41%) for diverticular bleeding. Among the entire study population, 112 (78.3%) patients had left-side diverticular disease, 7 (4.9%) left-side extended to trasverse colon diverticular disease and the remainig 24 (16.8%) had bilateral diverticular disease. Among patient who presented with diverticular bleeding (no. 59), 36 (61.0%) had left-side diverticular disease, 3 (5.1%) left-side extended to trasverse colon diverticular disease and remainig 20 (33.9%) had bilateral diverticular disease. On multivariate analysis, age 1.08 [1.04 – 1.12], male gender 4.80 [2.05 – 11.25] and bilateral divertcular diease 8.29 [2.38 – 28.79] were identified as risk factors independently related to dverticular bleeding. The relative risk for bleeding among patients with bilaterl diverticular disease was 2.56 [1.87 – 3.51].
**Conclusion:** Our preliminary findings suggest that bilateal diverticulosis was an independent risk factor for bleeding also in a western population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0407 IMPARED HUMAN COLONIC CONTRACTILITY AND TOLL-LIKE RECEPTOR 4 EXPRESSION IN UNCOMPLICATED DIVERTICULAR DISEASE

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**Introduction:** Uncomplicated Diverticular Disease (UDD) seems to be related to impaired intestinal motility, although it is still unknown whether the abnormal colonic motor activity is the primary event or the consequence of the presence of diverticula. In a recent study it has been shown that UDD induces significant modifications of Toll-like receptor 4 (TLR4) expression on several immune cell subpopulations isolated from both peripheral blood and affected mucosa. It is well known that during sepsis the activation of TLR4 impairs intestinal motility trough activation of intestinal muscolaris macrophages.
**Aims & Methods:** Therefore the aim of this study was to evaluate the contractility patterns in vitro of colonic smooth muscles strips (MS) and cells (SMC) obtained from human circular colonic muscle layers of UDD patients and to assess expression of Toll like receptors 4. Human colonic circular smooth MS or cells were isolated from specimens of human distal colon of 17 patients undergoing surgery for non-obstructive colonic cancer, among them 9 were found to have UDD. MS and SMC were exposed, after stabilitation, for 60 min to Krebs solution (control) and afterwards stimulated with a maximally effective dose of acetylcholine ($10^{-5}$M). Spontaneous phasic contractions on strips and morpho-functional parameters on cells were evaluated in basal conditions and in response to acetylcholine (Ach). Immunohistochemical staining for TLR4 was performed with goat polyclonal anti-TLR4 (Santa Cruz Biotechnology, Santa Cruz, CA, USA).
**Results:** Colonic MS of UDD group presented a significant reduced basal tone and Ach-elicited contraction over basal, compared to the results obtained in the control group (7.16 g and 47% in the DD group and 8.82 g and 69% in the CG, $p < 0.05$). Similarly to MS, SMCs of UDD group showed a mean resting cell length statistically higher than that obtained in CG ($158.7 \pm 12.1\,\mu m$ vs $184.8 \pm 12.9\,\mu m$, $p < 0.05$) with a maximal contractile response to acetylcholine significantly reduced when compared to controls, being 8, $831\% \pm 1.8$ vs $16.49\% \pm 1.2$, $p < 0.05$. At the epithelial level, in UDD patients, TLR4 was shown to be expressed mainly by scattered cells resembling enteroendocrine cells in colonic glands and only rarely by intestinal epithelial cells on the basolateral or apical surface. In the lamina propria and among smooth muscle cells, inflammatory cells were identified as main TLR4 expressing cells.
**Conclusion:** An impaired basal tone and contractility of circular colonic MS and SMCs was observed only in UDD patients group, compared to controls. The immunohistochemical analysis confirmed the expression of TLR4 both at the epithelial and at the lamina propria level, mainly on inflammatory and enterendocrine cells. It might be reasonable to hypothesize that in UDD the activation of TLR-4 plays a crucial role in inducing intestinal dismotility through production of cytokines by intestinal inflammatory cells and mediators by enteroendocrine cells.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0408 ASSESSMENT OF FECAL MICROBIOTA AND FECAL METABOLOME IN SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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**Introduction:** Pathogenesis of Symptomatic Uncomplicated Diverticular Disease (SUDD) is not completely understood. Imbalance of colonic microbiota is considered a milestone in occurrence of symptoms, but whether intestinal microbiota is really altered in those patients is unknown. Metabolic profiling is a powerful exploratory tool for understanding interactions between nutrients, the intestinal metabolism and the microbiota composition in health and disease, and metabolomics technologies have been applied for the screening of different pathological conditions that are linked with a metabolic imbalance.
**Aims & Methods:** We performed a prospective study assessing fecal microbiota and metabolome in symptomatic uncomplicated diverticular disease (SUDD). Stool samples from 52 consecutive female patients (17 with SUDD, 16 with asymptomatic diverticulosis (AD), and 19 healthy), born and living in the same geographic area, were analysed. Real-time PCR was used to quantify targeted microorganisms. High-resolution proton nuclear magnetic resonance spectroscopy in combination with Multivariate Analysis with partial least square discriminant analysis (PLS-DA) were applied on the metabolite data set.
**Results:** There were no differences in the demographic characteristics among the three groups. The overall bacterial quantity did not differ among the three groups. Thus, a colonic bacterial overgrowth was absent in SUDD ($p = 0.449$). In AD group a reduction in the percentage of Bifidobacteria and Enterobacteria and an increase of Clostridia and Lactobacilli compared to total bacteria was observed. These differences were however not significant. In both AD and SUDD groups a significant increase of Akkermansia muciniphila was also observed in comparison to healthy group ($p = 0.05$ and $p = 0.02$ respectively). PLS-DA analysis of NMR-based metabolomics of fecal waters showed a good discrimination between AD and SUDD patients ($R2 = 0.69$; $Q2 = 0.35$; $p < 0.05$). Moreover, significant differences in N-Acetyl-compounds were found between AD and SUDD patients. PLS analysis showed that SUDD patients, with higher N-Acetyl-compound levels as compared to AD patients, showed higher levels in Bifidobacteria and Enterobacteria, and lower levels in Clostridia and Lactobacillus spp.
**Conclusion:** SUDD does not show colonic bacterial overgrowth, but significant qualitative alteration of the fecal microbiota. Moreover, increasing expression of some metabolites as expression of different SUDD metabolic activity was found.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 10:30–17:00

## OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I – POSTER EXHIBITION

## P0409 H19 NON CODING RNA-DERIVED MIR-675, ACTIVATED BY HELICOBACTER PYLORI, PROMOTES GASTRIC CANCER FORMATION AND RESISTANCE TO CISPLATIN BY DOWNREGULATING FADD

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**Introduction:** H19 is increasingly described to play key roles in the development of cancers from different tissue origins. In this study, we aimed to find the association of H19 and *Helicobacter pylori*. In addition, the mechanism of H19 promoting gastric cancer formation and resistance was evaluated.
**Aims & Methods:** H19 expression in GC cells and tissues was quantified by quantitative reverse transcription-PCR (qRT-PCR). The GC cell lines were transfected with pc-H19, si-H19, or their respective controls and we investigated the phenotype of GC cells and possible molecular mechanisms.
**Results:** In this study, we established H19/miR-675 ectopic expression models of gastric cancer to further investigate the underlying mechanisms of H19 oncogenic action. We showed that overexpression of H19/miR-675 enhanced the aggressive phenotype of gastric cancer cells including increased cell proliferation, increased cell migration, decreased apoptosis and cisplatin resistance. In addition, H19 is overexpressed in cells cultured with *Helicobacter pylori*. Moreover, we identified FADD as direct targets of miR-675 in gastric cancer. Using a luciferase assay, we demonstrated that H19, through its microRNA, decreased FADD expression in gastric cancer cell. Thus, by directly binding FADD mRNA, miR-675 promotes gastric cancer, inhibiting activation of caspase-8 and caspase-3.
**Conclusion:** Our findings revealed that H19 is activated by *Helicobacter pylori* and can promote tumor formation and cisplatin resistance in GC and it will be a valuable predictor for treatment and target for reversal of cisplatin resistance in human GC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0410 HYDROTALCITE PROTECTS GASTRIC EPITHELIUM FROM DICLOFENAC-INDUCED INJURY BY UPREGULATING EGF-R, IGF-1 AND SURVIVIN: NEW MECHANISMS OF HYDROTALCITE'S PROTECTIVE ACTION AND THERAPEUTIC IMPLICATIONS

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**Introduction:** Diclofenac (DFN) is one of the most widely used NSAIDs worldwide. Clinical and experimental studies demonstrated that even a short term use of DFN induces gastric, duodenal and intestinal mucosal injury. Because of a wide spread use of DFN and side effects of long term PPI prophylaxis, it is very important to develop a new alternative strategy to counteract DFN's mucosal damaging actions. Hydrotalcite (HTL) - new generation antacid has been shown to protect gastric mucosa against ethanol injury, to accelerate gastric ulcer healing and is approved for clinical use in Europe, Canada and Asia. Our hypothesis was that HTL directly interacts with gastric epithelial cells, which are critical component of mucosal defense and upregulates expression of epidermal growth factor receptor (EGF-R), survivin and insulin like growth factor 1 (IGF-1), which in turn protect these cells from injury and death.
**Aims & Methods:** Our **aims** were to determine whether HTL can protect gastric epithelial cells from DFN-induced injury and to identify the underlying molecular mechanisms with focus on epidermal growth factor receptor (EGF-R), survivin (anti-apoptosis protein), and insulin like growth factor (IGF-1) – which all can potentially enhance cell survival. **Methods:** Cultures of normal rat gastric mucosal (RGM1) cells, which have many features of epithelial progenitor cells, were pretreated with placebo or HTL suspended in medium (1–5 mg/ml) for 1 - 4 hrs and then exposed to either: medium alone (controls), or sodium diclofenac (DFN; 0.5–1.0 mM) for 1–4 hrs. **Studies:** 1) cell injury under confocal microscope; 2) cell death/survival using novel Calcein AM live cell tracking dye; 3) expression of: EGF-R, survivin and IGF-1 by immunostaining and quantification of signal intensity using Metamorph 7 imaging system.
**Results:** DFN treatment of RGM1 cells caused very extensive cell injury and reduced cell viability from $95 \pm 3\%$ in controls to $12.7 \pm 4\%$; $p < 0.001$. Pretreatment of RGM1 cells with HTL significantly increased in these cells expression of EGF-R by 84%, survivin by 47% and IGF-1 by 72% (all $p < 0.001$) and significantly reduced/prevented DFN-induced RGM1 cells death; cell viability in this group was $71 \pm 6\%$, i.e. 5.7-fold higher ($p < 0.001$) than in medium + DFN treated group.
**Conclusion:** 1) Diclofenac induces extensive injury and death of gastric epithelial cells, which are critical component of gastric mucosal defense. 2) Treatment with hydrotalcite significantly upregulates in gastric epithelial RGM1 cells expression of EGF-R, survivin, and IGF-1 and protects these cells against diclofenac-induced injury. 3) These findings provide novel molecular mechanisms for DFN-induced gastric epithelial injury and HTL's protective action on gastric mucosal cells and a rationale for therapeutic use of HTL to prevent DFN-induced injury as alternative to proton-pump inhibitors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0411 EXPRESSION OF ALPHA ACTININ-4 IN SPINDLE CELL CARCINOMA OF THE ESOPHAGUS

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**Introduction:** Spindle cell carcinoma (SpCC) of the esophagus is a rare malignant neoplasm composed of both carcinoma and sarcomatous elements. The pathogenesis of the sarcomatous component of the tumor has not been elucidated. On the other hand, epithelial mesenchymal transition (EMT) is a phenomenon by which epithelial cells lose their property and turn into mesenchymal cells. It is said that EMT has various biological roles in tumor budding, including invasive front formation and sarcomatous change of epithelial cells. Recent studies have shown that alpha actinin-4, which is an isoform of non-muscular a-actinin and actin-bundling protein, plays an important role in cancer invasion and metastasis by enhancing cellular motility through EMT. However, most studies about alpha actinin-4 have focused on the invasiveness of tumor cells; it is unclear whether alpha actinin-4 is involved in the pathogenesis of the sarcomatous component in SpCC of the esophagus.
**Aims & Methods:** To investigate the involvement of alpha actinin-4 in sarcomatous differentiation, we performed immunohistochemistry for alpha actinin-4 in 14 cases of SpCC of the esophagus. We also evaluated E-cadherin, whose loss of expression is considered a hallmark of EMT. The stainings of alpha actinin-4 and E-cadherin in carcinoma and sarcomatous components were scored as follows: -, 0% of positive cells; +, 1–10%; ++, 11–50%; +++, 51–80%; and ++++, >80%. In order to verify the neoplastic nature of the sarcomatous component, we examined the monoclonality between carcinoma and sarcomatous elements, comparing TP53 mutation status and protein expression of both areas by DNA sequencing and p53 immunohistochemistry, respectively.
**Results:** Cytoplasmic alpha actinin-4 expression was more extensive in the invasive front of the carcinoma component than that in the sarcomatous component ($P = 0.0101$). Membranous E-cadherin expression was mostly lost in the invasive front of carcinoma areas and sarcomatous cells in all cases ($P < 0.0001$). The p53

expression pattern was almost concordant between the two components in all cases. TP53 mutation analysis uncovered that 7 cases possessed identical mutations in both areas. One case had mutations only in the sarcomatous component.
**Conclusion:** We found that alpha actinin-4 was significantly widely expressed in the invasive front of the carcinoma component compared to that in the sarcomatous component. We also found identical TP53 mutation patterns and nuclear p53 immunohistochemical staining in both carcinoma and sarcomatous areas. These findings suggest that the two components in SpCC of the esophagus have a monoclonal origin and alpha actinin-4 is involved in acquisition of invasiveness rather than in the formation of the sarcomatous component in SpCC of the esophagus.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0412 THE ACTIVITY OF H+/ K+ -ATPASE IN BIOPSY MATERIAL OF PATIENTS WITH GASTRIC ULCER

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**Introduction:** It is known that origin of a peptic ulcer in the stomach and in the duodenum is associated with disorders of interaction between factors of gastric juice aggression and mucosal protective properties. Acid-peptic factor is the most important in mechanisms of the gastric ulcer development. Its aggressiveness primarily associated with hydrochloric acid ulcerogenicity. The synthesis of this compound depends on the functioning of H+/K+-ATPase (the enzyme of the stomach mucous membrane parietal cells).
**Aims & Methods:** The aim of the study was the evaluation of H+/K+-ATPase activity in gastric mucosa biopsy material of patients in exacerbation and remission phase of *H. pylori*-dependent and *H. pylori*-independent duodenal ulcer (DU). 44 patients of the Institute of Gerontology of NAMS of Ukraine clinic (gastroenterological department) took part in the study (20 men, 24 women, 18–69 years old). Diagnosis and disease stage were endoscopically and morphologically verified. The presence of *H. pylori* infection in patients was confirmed by urease and histological tests and accounted 70%: 30%. The control group consisted of 10 volunteers (4 men and 6 women of the same age) with absence of duodenal ulcer in past history. Biopsy material from the fundus of the stomach was received (parietal cells with H+/K+-ATPase are localized here). Taking into account that H+/K+-ATPase activity does not depend on gender and age of patients we divided patients into 3 groups: 1st - healthy volunteers, 2nd - patients in exacerbation phase of DU and 3rd - patients in remission phase of DU. All patients received combined therapy with proton pump inhibitors and anti-Helicobacter pylori agents.
**Results:** It has been shown that in gastric mucosa biopsy material of patients in exacerbation phase of DU the activity of H+/K+-ATPase was 2.5 folds higher than in healthy volunteers. In remission phase the enzyme activity decreased by 1.3 folds as compared with patients in exacerbation phase of DU, but in the same times it was 2 folds higher than in healthy volunteers. Thereby, in spite of reparative processes in the gastric mucosa (according to the results of endoscopic and histological examination complete epithelization of the ulcer was observed) functioning of membrane-bound enzyme of gastric glands parietal cells remained to be impaired. It should be noted that in exacerbation phase activity of H+/K+-ATPase in patients with *H. pylori*-dependent form did not differ from the activity of the enzyme in patients with *H. pylori*-independent form.
**Conclusion:** Our results confirm the lack of association between the activity of H+/K+-ATPase and *H. pylori* and suggest that regenerative processes in the gastric mucosa in remission phase of DU occur in the absence of normalization of the functioning of parietal cells' H+/K+-ATPase. This factor increases the risk of new relapses. Thereby, search of approach aimed to correct H+/K+-ATPase activity have not lost topicality.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0413 IMAGING THE GLYCOME IN RAT STOMACH MUCOSA UNDER CONDITIONS OF ULCERATION AND PRETREATMENT WITH TRIPEPTIDE T-34

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**Introduction:** Due to their structural diversity and sensitivity to intra- and extracellular conditions, glycans are an indispensable tool for analyzing cellular transformations [1]. Glycome of rat stomach mucosa (SM) in health and ulceration leaves much to be elucidated.
**Aims & Methods:** Aim of our study was to assess changes of galactose-specific carbohydrate determinants of SM in indomethacin-induced (II) gastric lesions (GL) in rats, pretreated with tripeptide T-34 (H-Glu-Asp-Gly-OH).
Studies were conducted on white male rats due to international ethical regulars. Rats were devided into 3 groups: 1) control (n = 6); 2) intragastrically (ig) administered indomethacin (ind), (35 mg/kg, n = 6); 3) ig pretreated with T-34 (10 μg) 30 min before ind introduction (n = 6). 24 h later rats were sacrificed, SM was removed, fixed in 4% neutral formalin, and embeded in paraffin wax. SM glycome was studied by lectin-peroxidase technique. Intensity of lectin-receptor reaction was scored as follows: 0 – no reaction; 1 – weak; 2 – mild and 3 – strong reaction. Lectin panel is presented in Table 1.
**Results:** Ind caused erosive GL ($9.7 \pm 0.4$ mm$^2$), score of damage made $8.0 \pm 0.57$. T-34 effect resulted in tendency to decrease of GL area and diminished injury index ($p < 0.05$). We detected relatively faint reactivity of gastric mucosal epithelial barrier (GMEB) to HPA and PNA, whereas strong labeling by SBA-lectin. Concerning glandular cells of SM, HPA reactivity in chief cells was restricted only to T-34 –pretreated group. HPA-staining of parietal cells was evaluated as $1.83 \pm 0.34$ in control animals, $2.83 \pm 0.18$ – in II GL ($p < 0.05$) and $1.67 \pm 0.23$ in T-34-group ($p < 0.05$). Simultaneously increased number of HPA-positive cells was noted in II GL. HPA- and PNA-staining also revealed increased number of mucocytes in T-34-pretreated rats and enhanced binding affinity closer to foveola surface. Evaluation of cytotopography of receptors to PNA and SBA in glandular cells of SM showed increased reactivity to parietal cells in GL, which decreased in T-34-pretreated rats. Development of GL resulted in decreased SBA-labeling of mucocytes ($1.17 \pm 0.18$) compared to control ($1.83 \pm 0.18$, $p < 0.05$), that was not enhanced by T-34. All used lectins did not label endocrinocytes of stomach glands.

**Table 1:** Lectins and their respective carbohydrate specificities.

| № | Lectin designation, abbreviation | Specific monosaccharide | Complementary oligosaccharide/ polysaccharide |
|---|---|---|---|
| 1 | Peanut, PNA | DGal | DGal (β1-3) GalNAc |
| 2 | Soybean, SBA | αDGalNAc > βDGalNAc | GalNAc (α1-3) Gal (β1-3) GalNAc |
| 3 | Helix promatia, HPA | αDGalNAc | GalNAc (α1-3) GalNAc |

**Conclusion:** Cyclooxygenase-1/2 blockage by ind affects glycoconjugates processing in rat SM, decreasing αDGalNAc > βDGalNAc, DGal in mucocytes and increasing αNAcDGal, βDGal in parietal cells. SBA-lectin demonstrated the strongest affinity among galactose-specific lectins to GMEB. Cytoprotective effect of T-34 was accompanied by redistribution of II alterations of glucoconjugates, approaching glycome in control rats. Lectins may be used as a valuable molecular tool to explore functional peculiarities of SM cells in gastrointestinal disorders.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0414 EFFECT OF TRIPEPTIDE T-34 ON SYALO- AND FUCOSE-SPECIFIC CARBOHYDRATE DETERMINANTS OF STOMACH MUCOSA IN INDOMETHACIN-INDUCED GASTRIC LESIONS IN RATS

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**Introduction:** Recent research provides increasing evidence on gastroprotective effects of certain short peptides although their mechanism of action is under-investigated. Our previous studies revealed gastroprotective effects of hexapeptide thymohexin (Arg-α-Asp-Lys-Val-Tyr-Arg) and tripeptide T-34 (H-Glu-Asp-Gly-OH) in experimental gastric lesions (GL) associated with a decrease of nitrosooxidative stress in gastric mucosa (GM) [1, 2].
**Aims & Methods: Aim of research** was to assess the effect of T-34 on GM glycome. Studies were conducted on white male rats due to international ethical regulars. Rats were devided into 3 groups (n = 6 in each group): 1) control; 2) intragastrically (ig) administered indomethacin (ind), 35 mg/kg; 3) ig pretreated with T-34 (10 μg) 30 min before ind introduction. 24 h later rats were sacrificed. GM glycome was studied by lectin-peroxidase technique. Lectins panel included fucose- (Laburnum anagyroides bark agglutinin (LABA) and syalo-specific (Sambucus nigra agglutinin (SNA) and Wheat germ agglutinin (WGA). Intensity of lectin-receptor reaction was scored: 0 – no; 1 – weak; 2 – mild and 3 – strong reaction.
**Results:** We revealed strong reactivity of control animals GM both to syalo- and fucose-specific lectins although WGA/SNA-labeling was higher compared to LABA ($p < 0.05$). In intact rats expression of fucose-specific receptors was high in epitheliocytes, chief cells and mucocytes, whereas LABA-staining of parietal cells was low. In GL tendency to increased reactivity of epitheliocytes and decreased staining of chief cells and mucocytes was noted. T-34 pretreatment resulted in decrease of GL area, what was accompanied by decreased reactivity of epitheliocytes to LABA ($p < 0.05$) and interestingly reduction of fucose-specific receptors of mucocytes was even more significant ($p < 0.05$) compared to ind effect. T-34 also caused tendency to increased LABA-staining of chief and parietal cells ($p > 0.05$). No changes of epitheliocytes reactivity to WGA and SNA

were revealed between experimental groups. GM ulceration decreased affinity of chief cells and mucocytes to WGA compared to control, what was reversed by pretreatment of T-34. SNA-staining of epitheliocytes, chief cells and mucocytes in GL significantly decreased ($p < 0.05$). T-34 enhanced the reduction of syalospecific receptors of chief cells noted in ind-treated group.
**Conclusion:** Cyclooxygenase-1/-2 blockage by ind results in molecular transformation of GM glycans. The most significant changes were revealed in SNA-staining of epitheliocytes, chief cells and mucocytes of GM between experimental groups. Cytoprotective effect of T-34 reversed some ind-induced alterations of GM glycome but caused reduction of SNA-labeling of chief cells and LABA-labeling of mucocytes compared to control what may be speculated as masking of relevant receptors by other glycans. Molecular interaction between short peptides and GM glycans need deeper elucidation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0415 THE ROLE OF STOMACH DIFFUSE NEUROENDOCRINE SYSTEM AND PROLIFERATION IN REALIZATION OF CORREA CASCADE IN DISEASES ASSOCIATED WITH HELICOBACTER PYLORI


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**Introduction:** The aim of this study was to determine the role of vascular endothelial growth factor (VEGF), Ki-67, Bcl-2, and endocrine cells (EC) of the gastric mucosa (GM), producing somatostatin (SS), glucagon (GL), pancreatic polypeptide (PP) in diseases associated with *Helicobacter pylori* (*H. pylori*), and to supplement on their basis the early diagnostic criteria of GM structural changes progression in patients with gastric ulcer (GU), chronic atrophic gastritis (CAG), gastric adenomatous polyps (GAP) and gastric cancer (GC) before and after surgery, and *H. pylori* eradication therapy.
**Aims & Methods:** 104 patients with *H. pylori*-associated gastric diseases were enrolled in this study: 30 patients – with GU, 30 – with CAG, 20 – with GAP combined with CAG and 24 – with non-cardiac GC II (T1N2, T2N1, all M0) and III (T2N2, T3N1, T4N0 all M0) stages. The comparison group consisted of 12 healthy subjects. The material for morphological studies was taken from the antrum and fundus of the stomach. Immunohistochemical studies were performed using mouse monoclonal antibodies to VEGF, SS, GL, PP, Ki-67, Bcl-2. The number of Ki-67, Bcl-2, VEGF, SS, GL and PP - immunopositive cell nuclei automatically counted in 10 randomized fields of view.
**Results:** For acute GU reduction of EC number that produce VEGF, GL, PP and increasing of EC number producing SS (upon activation of proliferative processes, determined by immunopositive for Ki-67 and Bcl-2 EC number) were typical. After 2 months in GU remission normalization of all studied parameters of stomach diffuse neuroendocrine system and cell proliferation indicators was observed. CAG, GAP and intestinal type GC are associated with persistent *H. pylori* infection and accompanied by hyperplasia of EC secreting VEGF, GL, PP and hypoplasia of EC secreting SS, against the background of high proliferative activity of EC, expressed in terms of Ki-67 and Bcl-2.
**Conclusion:** VEGF, GL, SS and PP realizing their pathological properties directly or indirectly by *H. pylori*, Bcl-2, Ki-67 play an important role in predicting the occurrence and course of *H. pylori*-associated diseases. Eradication of *H. pylori* in the presence of intestinal metaplasia does not lead to its disappearance, therefore, all patients in need of dynamic observation, as well as persons who have this microbial expansion.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0416 COLLAGEN PEPTIDES PREVENT THE STRESS-INDUCED ULCERATION BY REGULATING STRESS-ASSOCIATED ACTIVATION OF NEUROENDOCRINE AND IMMUNE SYSTEMS


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**Introduction:** Interaction of the neuroendocrine and immune systems determines the ability of biosystems to resist the psychoemotional and physical strain. Hormones (adrenaline and cortisol in human, corticosterone in rats) enter the blood at stress. They are involved in the organism's adaptation to stress, however have ulcerogenic effect. The hormones excess in the blood causes activation of gastric secretion, HCl release, reducing the number of mucocytes and mucus production, which contributes to ulceration. Cortisol with time begins to depress the immune system and increases the risk of stomach ulcers, too. At stress is enhanced catabolism of collagen, a large number of short glycine- and proline-containing peptides fall into the blood. We showed that tripeptide Pro-Gly-Pro (PGP) and its acetylated derivative AcPGP, entered in various ways, reduce the stress-induced ulceration. But the mechanism of their gastroprotective action is not fully understood. We suggested that peptides can participate in the immune and neuroendocrine interactions.
**Aims & Methods:** I. We studied the effect of peptides - PGP and AcPGP - on the content stress hormones and the main pro-inflammatory cytokine in serum of rats after water-immersion stress (30 min, $t = 19–21^0$C). Intranasal injection of peptides (3.7 mmol/kg/40 ml) or saline solution was added 1 hour before ulceration. Blood was collected from the jugular vein of the rats to determine the production of adrenaline, corticosterone and IL-1$\beta$ by means of ELISA. II. We identify a local immune response in the stomach. Ln. gastricus caudalis of intact rats without ulcers (IR) and rats with stress ulcer (SU) were used as the source of T-lymphocytes. PGP or AcPGP ($10^{-5}$M) were added to the wells immediately after cell seeding. IL-1$\beta$ were determined in the supernatant of mononuclear cells after 24 h and 48 h.
**Results:** In serum IR were determined: adrenaline – $133.1 \pm 32.2$ ng/ml, corticosterone – $2.7 \pm 0.2$ ng/ml, IL-1$\beta$ – $22.51 \pm 5.5$ pg/ml. After stress adrenaline increased in 2 times, corticosterone in 4 times, IL-1$\beta$ in 5 times that reflects the high stress-tension of organism. Regional lymph node cells produced IL-1$\beta$ in 2 times higher at 24 hours after stress and after 48 hours less than IR cells. PGP and Acetyl-PGP prevent a sharp increase of hormones and the cytokine in the blood of rats in 1 h and in 24 h after stress in the supernatant of mononuclear cells.
**Conclusion:** Thus collagen peptides reduce of excessive stress-associated activation neuroendocrine and immune systems. Peptides regulate systemic and local immune response. Perhaps, this provides a good gastroprotection by stress-induced ulceration.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0417 HIGH DIAGNOSTIC PERFORMANCE OF A NOVEL ASSAY FOR AUTOANTIBODIES AGAINST ATP4A AND ATP4B SUBUNITS OF GASTRIC PROTON PUMP H+, K+-ATPASE IN ATROPHIC BODY GASTRITIS PATIENTS


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**Introduction:** The H+, K+-ATPase 4 of the parietal cells in the gastric oxyntic mucosa is a gastric proton pump maintaining an acidic environment within the stomach (1). Circulating autoantibodies, targeting the H+/K+-ATPase alpha (ATP4A) or beta (ATP4B) subunits, are considered diagnostic markers of autoimmune gastritis, but their real diagnostic utility is unclear. Previous studies employed enzyme-linked immunosorbent or indirect immunofluorescence to detect the autoantibodies against parietal cells, but did not discriminate reactivities against either the alpha or beta subunits (2, 3). Antibodies directed towards the H+, K+-ATPase 4B subunit (4) have not been assessed so far in patients with atrophic body gastritis, the histological condition associated with autoimmune gastritis.
**Aims & Methods:** The aim of this study was to assess the presence of autoantibodies against ATP4A and ATP4B subunits of parietal cells H+, K+-ATPase in patients with atrophic body gastritis and controls. Serum samples of 100 cases with histologically proven atrophic body gastritis (female 70%, median age 55 years) and 147 controls (female 79%, median age 45 years) were assessed for autoantibodies (IgG class) specific for either the ATP4A or ATP4B subunits by luminescent Immuno Precipitation System (LIPS). Recombinant antigens fused to a luciferase reporter were expressed by in vitro transcription and translation (ATP4A) or after transfection in Expi293F cells (ATP4B), incubated with test sera, and immune complexes recovered using protein A-sepharose. After addition of the luciferase substrate light output was measured in a luminometer and converted to arbitrary units using results from a positive serum as a reference. In addition, positive sera were titrated to properly quantify ATP4A and ATP4B autoantibodies. Cut-off values were selected using a normal-quantile plot analysis (ATP4A assay: $>51$ units; ATP4B assay: $>170$ units).
**Results:** Autoantibody titers were significantly higher in cases (ATP4A antibodies: median 3003 units, range 54–47, 429; ATP4B antibodies: median 2, 762

units, range 29–19, 796) compared to controls (ATP4A antibodies median units: 1, range 1–2, 440; ATP4B antibodies median units: 2, range 1–1, 301; $p < 0.0001$ for both assays). The area under the ROC curve of ATP4A and ATP4B assays was 0.98 and 0.99 ($p < 0.0001$ for both), respectively. Concordance between the two assays was good with a Spearman's coefficient of rank correlation (rho) 0.905 (95%CI 0.880 to 0.925, $p < 0.0001$). The ATP4A antibody LIPS assay showed a 100% sensitivity and 89.1% specificity and the ATP4B LIPS assay showed a 95% sensitivity and 97.3% specificity for atrophic body gastritis. Simultaneous positivity for both ATP4A and ATP4B autoantibodies in LIPS increased specificity for atrophic body gastritis (98.9% sensitivity and 97.04% specificity).
**Conclusion:** These novel assays for autoantibodies against ATP4A and ATP4B subunits showed a high diagnostic performance in atrophic body gastritis suggesting that oxyntic mucosa damage is strictly associated with gastric autoimmunity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0418 FROM THYROID AUTOIMMUNITY DISEASE TO AUTOIMMUNE CHRONIC ATROPHIC BODY GASTRITIS: POSSIBLE PREDICTOR MARKERS


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**Introduction:** Autoimmune chronic atrophic gastritis (ACAG) is often associated to the presence of other autoimmune disorders such as autoimmune thyroid disease (ATD); it has been demonstrated that this could be due to an immunological cross-reaction caused by the presence of an homologous auto-epitope between thyroperoxidase (TPO) and gastric parietal cell (PCA) antibodies.
**Aims & Methods:** To evaluate the role of predictive markers for ACAG in patients affected by ATD. A consecutive series of 1524 patients (441 males, 1083 females, mean age 44 years, range 6–89) selected from general population on the basis of dyspeptic symptoms was submitted to serum Pepsinogen I, II (PGI, PGII) and Gastrin 17 (G17) (Biohit, Plc) assays for ACAG identification. Among them, 309 patients who presented a clinical and immunological history of ATD (positivity for TPO antibodies, Siemens) were evaluated for PCA antibodies by indirect-immunofluorescence method (Menarini). Definitive diagnosis of CAG was performed by histological evaluation (OLGA Staging System).
**Results:** 39/94 (41.5%) of patients with ACAG were also affected by ATD. Table illustrates the results obtained from the following groups of patients:.

| | No ATD, No ACAG | ATD | ACAG | ATD + ACAG |
|---|---|---|---|---|
| **Patients** | 1082 | 309 | 55 | 39 |
| **Mean Age (ys)** | 42.3 | 43.7 | 57.9 | 54.3 |
| **Sex (M/F) (M:F)** (1:1.8) | 387/695 (1:1.8) 3/36 (1:12) | 298/280 (1:10) | 19/36 | |
| **PCA+** | 7 (0.7%) | 87 (28.1%) | 40 (72.7%) | 37 (94.9%) |
| **PCA-** | 1075 (99.3%) | 222 (71.9%) | 15 (27.3%) | 2 (5.1%) |
| **PGI (ug/L)** | 108.6 | 105.4 | 14.0 | 11.0 |
| **PGI/PGII (ratio)** | 12.6 | 12.0 | 2.3 | 1.5 |
| **G17 (pmol/L)** | 5.2 | 8.4 | 53.5 | 56.2 |

**Conclusion:** ATD and ACAG seem to occur in a closely linked fashion. ATD PCA negative young females have to be regularly monitored for PCA; ATD PCA positive young women should be followed up by gastric serological markers in order to early evidence a possible onset of ACAG.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0419 A POSSIBLE ROLE OF TYPE 1 INNATE LYMPHOID CELLS IN THE RECTAL MUCOSA OF PATIENTS WITH NON-CELIAC WHEAT SENSITIVITY


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**Introduction:** Non-celiac wheat sensitivity (NCWS) is a ''new'' and still undefined clinical condition. Its pathogenesis is incompletely understood, we evaluated the inflammatory response in the rectal mucosa of patients with well-defined NCWS.
**Aims & Methods:** The prospective study included 22 patients with irritable bowel syndrome (IBS)-like clinical presentation, diagnosed with NCWS by double-blind placebo controlled challenge. Eight IBS patients not improving on wheat-free diet were used as controls. Two-weeks after oral challenge, cells were isolated from rectal biopsies and thoroughly characterized by FACS analysis for intracellular cytokines and surface markers.
**Results:** Rectal biopsies from wheat challenged NCWS patients showed a significant mucosal $CD45^+$ infiltrate consisted of $CD3^+$ and $CD3^-$ lymphocytes, with these latter spontaneously producing more IFN-g than IBS controls. About 30% of IFN-g-producing $CD45^+$ cells were T-$bet^+$, $CD56^-$, $NKP44^-$ and $CD117^-$, defining them as a type-1 innate lymphoid cells (ILC1). IFN-g-producing ILC1 cells significantly decreased in ten patients analyzed two weeks after they resumed a wheat-free diet.
**Conclusion:** These data indicate that in patients with active NCWS, IFN-g-producing ILC1 cells infiltrate rectal mucosa and support a role for this innate lymphoid cells population in the pathogenesis of NCWS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0420 STUDY OF VARIATION BETWEEN THE ENDOSCOPIST, PATHOLOGIST AND THE BIOCHEMIST IN THE DIAGNOSIS OF CHRONIC FUNDAL ATROPHIC GASTRITIS: THERE IS NEED FOR DEFINITIVE GUIDELINES


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**Introduction:** Gastritis is a common condition and is diagnosed endoscopically and /or with histology. There are also biochemical markers available to differentiate different types of gastritis. There have been different classifications of Gastritis as types A, B and C and acute or chronic. More recently Sydney classification of gastritis has been introduced. The Endoscopists recognise mucosal atrophy by thinning of the mucosa which shows underlying blood vessels. The histopathologist looks for signs of duct dilatation, fibrosis, intestinal metaplsia and crypt changes in the lamina propria. The biochemist recommend that serum Pepsinogen I levels should drop in patients with fundal atrophy due to damaged chief cells. No previous study has looked at the concordance between these three modalities of diagnosis. This study aims to look at any relationship and degree of variation amongst the endoscopists, histopathologists and the biochemists in making the diagnosis of chronic fundal atrophic gastritis.
**Aims & Methods:** Endoscopy was performed on 71 patients by an experienced consultant gastroenterologist. Pre-endoscopy fasting samples were taken for Serum Pepsinogen I levels and two biopsies were taken from the fundus. If atrophic gastritis was suspected endoscopically, then the histopathologist was advised of the diagnosis in writing. Clo test was done on all patients. Senior histopathologists reviewed the histology slides and reported their findings. Serum Pepsinogen I level was done in Finland by Biohit laboratories and the sample was either stored at -20 degree Centigrade or treated with stabilizer to ensure validity during storage and transport. The study was done with approval

of the ethics committee and patient consent was obtained for participation. Patients were either on no PPIs or were off them for one week or a correction factor was put in case of their inability to be off the PPI due to worsening symptoms.
**Results:** 65 patients had some positive findings during endoscopy. 06 patient had normal endoscopy so histology samples were not undertaken for them but serum Pepsinogen I level was still undertaken. 40 patients had no fundal atrophy while 25 were deemed by the endoscopist to have atrophy. There was total agreement between the endoscopist and histopathologist in all 40 cases with no atrophy. However the histopathologist agreed with only 04 out of 25 cases diagnosed fundal atrophy by the endoscopist (84% disagreement) p value $< 0.019$. The biochemists likewise showed normal levels of Pepsinogen I in patients without fundal atrophy diagnosed by the endoscopist and the histopathologist in 39 out of 40 cases (97.5% agreement). However in patients with chronic fundal atrophy only 1 out of 25 patients had low Pepsinogen I when matched by the endoscopist's findings (96% disagreement) p value $< 0.625$ and in 0 out of 25 of them when matched with histopathologist's diagnosis. (100% disagreement) p value $< 0.880$.
**Conclusion:** This study has demonstrated that when chronic fundal atrophic gastritis is not suspected by the endoscopist, all three modalities of diagnosis i.e the endoscopist, histopathologist and the biochemist with biomarkers get an almost complete agreement. However when atrophy is suspected there is wide variation between the endoscopist, histopathologist and the it biochemist. Early recognition of fundal atrophy is important as it indicates a higher risk of developing cancer. Therefore a co-ordinated approach by the three may enable a more definitive diagnosis. There is need for clear guidance and training on endoscopic appearances of gastritis. Sydney Classification helps the histopathologist to a certain extent. Pepsinogen I as a biomarkers of gastric fundal atrophy has been validated and can become an important tool in helping the endoscopist and the histopathologist in making a more definitive diagnosis. If normal level of serum Pepsinogen I is taken as a guide prior to endoscopy, the endoscopist and the histopathologist, both can be more sure that there is no fundal atrophy and may achieve greater concordance in their reports. Further formal guidelines on diagnosis of various types of gastritis are warranted.
**Disclosure of Interest:** T. Mahmood: Biohit transported and conducted biochemical testing free of charge to Finland.

## P0421 THE USE OF CANCER-ASSOCIATED AUTOANTIBODIES AS BIOMARKERS IN GASTRIC MALIGNANCIES

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**Introduction:** According to GLOBOCAN, gastric cancer (GC) remains the third deadliest malignancy worldwide with Eastern Asia and Eastern Europe being the regions of the highest incidence and mortality. High-titer IgG class autoantibodies generated against tumor associated antigens have been demonstrated to have valuable biomarker qualities in various malignancies including GC[1] and have been used for non-invasive biomarker assay development[2].
**Aims & Methods:** In our previous study, we developed a recombinant tumor antigen microarray and data analysis algorithm suitable for robust autoantibody profiling and biomarker identification[3]. Within this study, we used these tools to reassess the diagnostic and prognostic value of 105 previously selected markers and evaluate possible inter-population differences in seroreactivity patterns by testing serum samples from GC patients and healthy controls (HC) (245 and 310 from Baltic States, and 296 and 298 from Taiwan, respectively). For prognostic analyses, autoantibody reactivity was compared in patients with available overall survival data subdividing them into long-term survival (LTS) group ($>1$ year, $n = 163$) and short-term survival (STS) group ($\leq 1$ year, $n = 28$).
**Results:** The study identified 26 and 33 autoantibody biomarker signatures in Taiwan and Baltic cohorts, respectively, capable of discriminating GC from HC in both cases with AUC of 0.6 ($p < 0.001$). Results revealed minor differences in antigen seroreactivity patterns between the Taiwan and Baltic cohorts, but indicated differences in immunodominant epitope prevalence for tumor antigens NY-ESO-1 and TP53. GC-associated serum autoantibodies were not statistically significantly associated with cancer stage, histological type, grade, *H. pylori* status, age or sex. However, a 15-autoantibody signature associated with worse prognosis was identified ($OR = 3.36$, $p = 3.3\,e\text{-}5$) and included serological responses against known tumor antigens such as MYC, MUC1, IMP1 and IMP2, while antibodies against NY-ESO-1, SSX2 and SOX2, amongst others, were found to be associated with longer overall survival.
**Conclusion:** Tumor antigen associated autoantibody repertoires show slight differences when compared between Caucasian and Asian cohorts. Although readily detectable at first stages of GC, the cancer-associated autoantibodies have limited diagnostic value, but may have possible clinical application as an independent prognostic factor.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0422 ORAL INTAKE OF PURIFIED AQUEOUS SOLUTION OF OAT B-GLUCANS HAS NO EFFECT ON GASTRIC MUCOSA HISTOLOGICAL CHANGES IN PATIENTS WITH CHRONIC GASTRITIS: A PILOT PHASE II CLINICAL TRIAL

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**Introduction:** Many studies have been shown, that $\beta$-glucans is effective as a natural immunomodulator and could be used as dietary supplement to reduce inflammation and oxidative tissue injury.
**Aims & Methods:** The aim of this study was to determine the effect of high or low molecular weight oat $\beta$-glucans on gastric mucosa histological changes in patients with chronic gastritis. Study participants were recruited from patients who underwent an elective esophagogastroduodenoscopy (EDG) due to dyspepsia. All consecutive eligible patients with initial diagnosis of gastritis within gastric antrum were invited to participate in the study. 48 patients were either randomly assigned to a placebo group, receiving an oral dose of 100 ml 3% solution of potato starch (P), or to one of the treatment groups receiving oral dose of 100 ml high molecular weight $\beta$-glucans (G1) or low molecular weight $\beta$-glucans (G2). Easily digestible diet was recommended for all groups. All participants underwent a baseline screening assessment which included a medical history and physical examination. Appearance of the mucosa of the stomach, and duodenum was evaluated and scored with the use of esophagogastroduodenoscopy scores (EGs) which were partially based on the Sydney grading/scoring system. Double biopsies for urease testing (GUT Plus, Poland) and histology were taken: pylorus, distal lesser curvature and the distal greater curvature. Endoscopy with biopsies and histological examinations were performed before treatment and the day after discontinuation of the administration the beta-glucan supplement. Plasma TNF-alpha and C-reactive protein (CRP) level was measured using ELISA kits (Merck Millipore, Germany).
**Results:** There were no statistically significant differences in CRP and TNF-alpha level as well as antral histological scores of inflammation, activity, atrophy, metaplasia and degree of *H. pylori* observed both within and between groups after 30 days of oral administration of beta-glucans.
**Conclusion:** Dietary supplementation with $\beta$-glucans did not reduce inflammation changes in patients with chronic gastritis. Although strong anti-inflammatory effect of oral $\beta$-glucans in gastrointestinal tract have been seen in animal models we could not confirm these effect in patients with chronic gastritis. Considering the underlying mechanism, the main reason could be that, in contrary to our population treated, in an animal model of GI inflammation the induced inflammatory process was rather acute with predominance of granulocyte infiltration. It would be of interest to further explore the exact effects of oral beta-glucans treatment in humans suffering from acute inflammation within GI tract like e.g. acute gastritis or ulcerative colitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0423 THE PREVALENCE OF ANTI-PARIETAL CELL AND ANTI-INTRINSIC FACTOR ANTIBODIES, PEPSINOGENS AND GASTRIN-17 IN CORPUS-RESTRICTED GASTRITIS PATIENTS

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**Introduction:** Corpus-restricted gastritis (usually of autoimmune origin) may result in pernicious anaemia as well as gastric cancer. The aim of our study was to detect the prevalence and values of anti-parietal cell antibodies (anti-PCA), anti-intrinsic factor antibodies (anti-IFA), pepsinogen ratio (PGI/II) and gastrin-17 (G-17) in corpus-restricted gastritis and control group patients.
**Aims & Methods:** This was a sub-group analysis of 1978 patients being referred for endoscopy due to dyspeptic symptoms; 5 biopsies were analysed according to updated Sydney system. ELISA method was used to measure PGI/II and G-17 (Biohit, Oyj., Finland); anti-PCA and anti-IFA (Inova Diagnostics, USA) in plasma samples. Spearman's correlation was run to assess the relationship between the biomarkers.

**Results:** 52 patients with corpus-restricted gastritis according to the morphology report were included to the study group and 104 patients without gastric atrophy in the control group. In the corpus-restricted gastritis group 59.6% and 9.6% patients were anti-PCA and anti-IFA positive with mean values of 45.0 and 13.7 units; in the control group 15.4% and 1% patients were anti-PCA and anti-IFA positive with mean values of 10.8 and 5.8 units, $p < 0.001$ and $p = 0.184$ respectively. There was a strong negative correlation between G-17 and PI/II ratio ($rs = -.731$, $p < .001$), a positive correlation between G-17 and anti-PCA ($rs = .325$, $p < .001$) and a negative correlation between PI/II ratio and anti-PCA ($rs = -.320$, $p < .001$).
**Conclusion:** Increased anti-PCA levels were observed in a significant proportion of patients with corpus-restricted gastritis. In contrast, anti-IFA levels increased in only a small proportion of patients. There was a negative correlation between G-17 and PI/II ratio and between anti-PCA and PI/II ratio, while a positive correlation between G-17 and anti-PCA values was observed.
**Disclosure of Interest:** Z. Shums: Employee of Inova Diagnostics Inc, San Diego, CA, USA.
G.L. Norman: Employee of Inova Diagnostics Inc, San Diego, CA, USA.
All other authors have declared no conflicts of interest.

## P0424 THE PREVALENCE OF AUTOIMMUNE GASTRITIS IN CAUCASIANS WITH GASTRIC ADENOCARCINOMA

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**Introduction:** Gastric atrophy and *H. pylori* infection are well-known risk factors of gastric adenocarcinoma, but the relevance of autoimmune gastritis in gastric adenocarcinoma development is not entirely clear.
**Aims & Methods:** We studied anti-parietal cell antibodies (anti-PCA) and anti-intrinsic factor antibodies (anti-IFA) levels and their associations with pepsinogen PgI/PgII levels in Caucasian patients with morphologically confirmed gastric adenocarcinoma. Plasma levels of anti-PCA and anti-IFA were measured by ELISA (Inova Diagnostics, USA), the cut-off value for both was ≥25 units. Plasma levels of PgI, PgII, *H. pylori* IgG were measured by ELISA (Biohit, Oyj., Finland). A cut-off value of PgI/PgII <3 was used to detect gastric atrophy. The cut-off value for *H. pylori* IgG was ≥30 units.
**Results:** A total of 229 patients (134 men, 95 women, median age 65, range: 35–86) with confirmed gastric adenocarcinoma from Riga East University Hospital in Latvia were included to the study. Positive autoantibody (either anti-PCA or anti-IFA or both) was found in 25 (11%) of the patients with adenocarcinoma, the positivity results for each subgroups are provided in the Table. Significantly, higher prevalence was found in the group with pepsinogen values characteristic for gastric atrophy.

| | *H. pylori* IgG | PgI/PgII ≥ 3 | PgI/PgII < 3 | P-value (Pg subgroups) |
|---|---|---|---|---|
| Positive anti-PCA (n = 24) | 9 (38%) | 8 (33%) | 16 (67%) | 0.0003 |
| Positive anti-IFA (n = 6) | 1 (17%) | 1 (17%) | 5 (83%) | 0.0134 |
| Positive both (n = 5) | 0 (0%) | 1 (20%) | 4 (80%) | 0.0368 |
| Positive anti-PCA or anti-IFA or both (n = 25) | 10 (50%) | 8 (32%) | 17 (68%) | 0.0002 |

**Conclusion:** Autoantibodies suggesting the presence of autoimmune gastritis were detected in only a minority of patients with gastric cancer, with only 1 of 9 (25/229) patients presenting with positive test results suggesting the presence of autoimmune gastritis. As expected, presence of autoantibodies is higher in atrophic gastritis group.
**Disclosure of Interest:** Z. Shums: Employee of Inova Diagnostics Inc, San Diego, CA, USA.
G.L. Norman: Employee of Inova Diagnostics Inc, San Diego, CA, USA.
All other authors have declared no conflicts of interest.

## P0425 REDUCED 25-OH-VITAMIN D LEVELS IN PATIENTS WITH CHRONIC AUTOIMMUNE ATROPHIC GASTRITIS

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**Introduction:** chronic atrophic autoimmune gastritis (CAAG) is an organ-specific autoimmune disease characterized by the presence of autoantibodies against gastric parietal cells or intrinsic factor. The progressive destruction of the parietal cells leads to hypo/achlorhydria and results in a reduced absorption of vitamin B12. The possible role of CAAG and gastric achlorhydria in the pathogenesis of several nutritional deficiency has already been reported. Moreover, few studies reported the possible association between CAAG and 25-OH-Vitamin D deficiency.
**Aims & Methods: Aim:** To evaluate the prevalence of 25-OH-Vitamin D deficiency in a cohort of patients affected by chronic atrophic autoimmune gastritis.
**Methods:** 25-OH-Vitamin D, PTH, calcium and ionized calcium were measured in all the patients with atrophic gastritis followed at our center from January 2012 to July 2015. Results were compared with a control group formed by 1402 subjects [1093 females, 309 males; median age 62 years (14–83)]. Patients with primary hyperparathyroidism, abnormal calcium values or renal failure were excluded.
**Results:** 86 CAAG patients (64 females; median age 65 years) were studied. Median 25-OH-vitD was significantly lower than in the control group (17.9 vs 23.9 ng/ml, $p < 0.0001$). 25-OH-VitD deficiency was observed in 57 patients (66%) considering 20 ng/ml as a cut-off and in 22 patients (26%) considering 12.5 ng/ml. In detail, 25-OH-vitD was significantly lower in CAAG patients compared with controls in decades 36–45 (17.7 vs 22 ng/ml, $p = 0.02$), 46–55 (17 vs 22.5 ng/ml, $p = 0.03$), 56–65 (18.7 vs 24.2 ng/ml, $p = 0.0043$), 66–75 (17.7 vs 24.3 ng/ml, $p < 0.0004$) and 76–85 (13.9 vs 24.3 ng/ml, $p = 0.003$). No differences were observed for decades below 35 and above 86 years probably due to the low number of patients in these groups. The two groups don't differ significantly for age and male/ female distribution.
**Conclusion:** the increased incidence of osteopenia and osteoporosis in patients with longstanding hypochlorhydria has already been reported. Moreover, few studies reported a reduction in calcium and phosphorus levels in patients with hypochlorhydria. To the best of our knowledge this is the first study aimed at evaluating 25-OH-Vitamin D levels in patients affected by CAAG. Our study, showed 25-OH-Vitamin D levels significantly reduced in patients with CAAG as compared to control group. These observations suggest a possible impairment in vitamin D absorption in CAAG's patients, which could lead to alteration in bone mineralization.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0426 PROGNOSIS OF ENDOSCOPIC HEMOSTASIS FOR THE GASTROINTESTINAL BLEEDING ULCER WAS DEPENDENT ON THE CHARACTERISTICS OF THE PATIENTS, BUT NOT ON CORRESPONDENCE OF THE MEDICAL STAFFS IN JAPAN

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**Introduction:** Endoscopic hemostasis is the first therapeutic approach to the emergent upper gastrointestinal bleeding, which is the still serious life-threatening condition. The present study aimed to examine i) whether visiting time to the hospital influenced prognosis of the outpatients with the bleeding peptic ulcer, and ii) whether prognosis of the outpatients who received endoscopic hemostasis was different from that of the hospitalized patients.
**Aims & Methods:** Totally, 444 patients who received emergency endoscopic hemostasis from January, 2008 to December, 2014 were included in the present study. These patients were divided into two groups of hospitalized patients (137 cases) and outpatients (307 cases). The outpatients were divided into two semi-groups; the group A of 120 cases who visited the hospital in time (8:30 to 17:00 on weekdays), and the group B of 187 cases in out of the regular consultation time (17:00 to 8:30 on 0weekdays or holidays).
**Results:** Backgrounds of the outpatients including age, gender, underlying disease, and medication were not different between the groups A and B. The treatment outcomes of endoscopic hemostasis for the bleeding ulcer including primary hemostasis, re-bleeding, complications, and number of deaths within one month were not different between the groups A and B. Compared to the outpatients, mortality rate ($p < 0.01$), recurrent bleeding rate ($p < 0.01$), and procedure related accident rate after endoscopic hemostasis ($p < 0.01$) were relatively high in the hospitalized patients. The average age of the hospitalized patients was old compared to the outpatients ($p < 0.01$), and severe comorbidity was complicated in the hospitalized patients with the bleeding peptic ulcer; diabetes mellitus ($p < 0.01$), cerebrovascular disease ($p < 0.01$), and malignant neoplasm ($p < 0.01$). The significant mortality risks of the hospitalized patients compared to the outpatients were aging more than 65 year old ($p < 0.01$), and complicated malignant neoplasm ($p < 0.05$).

**Conclusion:** The present study indicated the prognosis of the patients with the bleeding peptic ulcer who were treated by the endoscopic hemostasis was better in the outpatients compared to the hospitalized patients, and the prognosis was not influenced the visiting time to the hospitals. These results suggest that prognosis of endoscopic hemostasis for the upper gastrointestinal bleeding might be dependent on the characteristics of the patients, but not on correspondence of the medical staffs including the endoscopists.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0427 INFORMATICS ASSESSMENT OF BURDEN OF ANAEMIA POST UPPER GI BLEEDING IN AN UNIVERSITY HOSPITAL POPULATION

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**Introduction:** Upper GI bleeding (UGIB) remains a considerable burden causing premature mortality throughout the world. Uncertainty exists about the best haemoglobin measure to aim for acutely and on discharge in order to prevent premature mortality. However, the long term effects of anaemia post-UGIB has not been evaluated in secondary care cohorts, particularly to assess associations with mortality and the potential role of risk factors.
**Aims & Methods:** In order to assess the associations of anaemia post-UGIB, we analysed the secondary care patient sample identified from University Hospital Birmingham informatics electronic patient records databases, which has a catchment population of just over half a million in South Birmingham. Demographics, clinical and follow-up information were collected on first admission per patients having: (i). an upper gastrointestinal endoscopic procedure; (ii). a haemoglobin measurement; and (iii). an admission between 1st January 2010 and 31st December 2014. Anaemia status was defined using the last haemoglobin (Hb) measurement before discharge according to high (Hb $>=$10) or low (Hb $<$ 10). Upper GI bleeding and related conditions were detected using ICD10 codes: Gastric K25, Duodenal K26, Peptic K27, GI bleeding K92, Varices I85. One year survival post discharge was collected from UHB regional databases and was analysed using log rank statistics in Kaplan Meier survival curves. A naïve analysis of all data was compared against a matched analysis where patients were matched on propensity to anaemia using risk factors in a generalised logistic model.
**Results:** There were 1304 cases of upper GI bleeding identified in the 5 year period. The median range of patients was 67 years (interquartile range 54–80 years). 38.6% (504) of patients were female. Ethnicity included: Caucasian 81.7% (1065), South Asian 9.3% (121), and Other 9.0% (118). Prevalence coding of past and current medical history was predominantly Peptic ulcer (50.3%) but also included: Liver disease (18.8%); Diabetes Mellitus (16.9%); Cancer (16.6%); Renal disease (15.5%); Myocardial Infarction (12.1%); and Congestive Cardiac Failure (9.5%). Independent risk factors for overall mortality identified included: admission method (emergency or elective; $p < 0.0001$), age ($p = 0.0005$), gender ($p < 0.001$), body mass index ($p < 0.001$) and comorbidities (liver disease, renal disease, peptic ulcer all $p < 0.001$; heart failure and diabetes $p < 0.02$). One year survival between those discharged with a Haemoglobin $>=$10 and $<$10 when adjusted for age, gender, admission method, demographics, body mass index was 85.1% versus 76.7% ($p = 0.0034$). However, when comorbidities were also adjusted for, there was limited evidence to suggest overall mortality differences between high and low Hb groups ($p = 0.31$).
**Conclusion:** This large-scale informatics study in a single centre secondary care population has identified associations post-UGIB for a 1 year mortality difference dependent on haemoglobin on discharge. However, this appears to be associated with comorbidities rather than anaemia per se. Further studies to assess the long-term effects of post-UGIB anaemia are required.
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## P0428 INCIDENCE, CLINICAL CHARACTERISTICS AND RISK FACTORS OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS ON DUAL ANTI-PLATELET THERAPY AFTER PERCUTANEOUS CORONARY INTERVENTION IN SOUTH CHINA

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**Introduction:** The acute coronary artery syndrome (ACS) patients should take aspirin and clopidogrel (dual anti-platelet) for at least 1 year after percutaneous coronary intervention (PCI). However, dual anti-platelet therapy in patients increases the risk of gastrointestinal bleeding (GIB), hospitalization time and costs, and adverse clinical outcomes. It has been reported that, the risk factors of GIB after PCI include old age[1], female[2], smoking[2], drinking[2], taking non steroidal anti-inflammatory[1]and anticoagulant drugs[1], with digestive tract tumors[3], congestive heart failure[3], low BMI[4], renal inadequacy[5], coronary artery bypass graft[6], previous history of peptic ulcer[1, 2] and bleeding[1, 2].Proton pump inhibitors (PPI) can prevent and treat the upper GIB (UGIB) after PCI. But there has not any statistical data about UGIB after PCI for 1 year in China, and the lifestyle and genetic characteristics are different from foreign patients; this study intends to provide help for the prevention and treatment of UGIB after PCI.
**Aims & Methods:** To investigate the incidence, clinical characteristics and risk factors of UGIB in ACS patients on aspirin with clopidogrel dual anti-platelet therapy after PCI. Clinical data of ACS patients who had undergone PCI in the cardiovascular institute of Guangdong General Hospital from Sep 2009 to Aug 2014 were reviewed. The incidence of UGIB and clinical characteristics of ACS patients on dual anti-platelet therapy for 1 year after PCI were analyzed. Risk factors of UGIB were screened by comparing the cases and controls, which were trebly matched with the same age and sex.
**Results:** 9118 ACS patients had undergone PCI and UGIB occurred in 189 patients (2.07%) totally from Sep 2009 to Aug 2014. Except those happened over one year, with digestive tumors or varices and negative results under endoscopy, UGIB occurred at a rate of 0.61% in 56 patients (0.61%) and appeared to decline year by year. Most patients (91.07%) had melena or stool occult blood positive, while others had bloody stool or haematemesis. Most UGIB were ulcer-related under endoscopy, which accounted for 67.86%, and there were 24 duodenal ulcers and 13 gastric ulcers and 1 complex ulcer, while others were gastric erosion, gastritis and duodenal bulb. The risk factors of UGIB were previous history of peptic ulcer ($P < 0.01$) and renal inadequacy ($P < 0.01$), while PPI use was a protective factor ($P < 0.05$). The incidence of new-onset ACS was 1.44% with PPI use, and 1.34% without PPI use; there was no significant difference between the two groups ($P > 0.05$). PPI use for prevention of UGIB after PCI didn't increase the incidence of ACS.
**Conclusion:** UGIB occurs at a rate of 0.61% in ACS patients on dual anti-platelet therapy (aspirin and clopidogrel) for 1 year after PCI and appears to decline year by year. PPI use after PCI contributes to preventing UGIB, especially for those who had precious history of peptic ulcer and renal inadequacy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0429 SHORT-TERM USE OF GINKGO BILOBA INCREASE RISK OF UPPER GASTROINTESTINAL BLEEDING: A NATIONWIDE POPULATION-BASED CASE-CROSSOVER STUDY

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**Introduction:** Ginkgo biloba (ginkgo) has been widely used to treat dementia, cognitive impairment, peripheral nerve problems and vascular tinnitus worldwide. To our knowledge, whether Ginkgo increases risk of upper gastrointestinal bleeding still remains unknown.
**Aims & Methods:** To clarify whether Ginkgo increases risk of upper gastrointestinal bleeding and identifies the risk modifiers. This was a national population-based study by using National Health Insurance database (NHIRD) of Taiwan and conducted with the case cross-over study design with time windows of 7, 14 and 28 days. According to the Taiwan National Health Insurance database, patients aged >20 year old and <95 year old and hospitalized for upper gastrointestinal hemorrhage during January 1, 2000 to December 31, 2012 were retrieved according to ICD-9-CM diagnosis codes with endoscopic therapies from inpatient claims from the one million random sample of NHIRD. Those who ever used Ginkgo (>=1 day) before admission were defined as Ginkgo-indicated patients. A conditional logistic regression model was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). Test interaction test was performed to determine the risk modifier of Ginkgo related upper gastrointestinal bleeding.
**Results:** A total of 13752 patients with upper gastrointestinal bleeding were retrieved and 1504 Ginkgo-indicated patients were analyzed. The odds ratio for the risk of upper gastrointestinal bleeding and risk of severe bleeding in need of blood transfusion after Gingko exposure were 5.21 (95% CI, 2.94–9.24) and 7.83 (95% CI, 3.35–18.32) for the 7-daywindow, 2.45 (95% CI, 1.59–3.77) and 3.39 (95% CI, 1.82–6.28) for the 14-day window, and 1.85 (95% CI, 1.31–2.63) and 1.78 (95% CI, 1.11–2.85) for the 28-day window respectively. The test of interaction showed the risk of Gingko-related UGI bleeding existed regardless of age, gender, comorbidities and concurrent medicines.
**Conclusion:** Short- term Ginkgo use increased the risk for upper gastrointestinal bleeding, especially within 7 days and had lag effect up to 28 days, regardless of age, gender, comorbidities and concurrent medication.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0430 CHADS2 SCORE IS A PREDICTOR OF DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS

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**Introduction:** Delayed bleeding is one of major complications associated with endoscopic treatment for gastrointestinal neoplasms. Some predictors are known to involve in delayed bleeding after endoscopic treatment, and however, the association between CHADS2 score and delayed bleeding after gastric ESD has not been reported.
**Aims & Methods:** The present study aimed to identify the predictors of delayed bleeding after gastric ESD. Data of consecutive inpatients who underwent ESD for gastric neoplasms in Osaka General Medical Center between January 2013 and March 2016 were retrospectively investigated. Main survey item was delayed bleeding, and we also investigated the associated factors, including age, gender, characteristics of lesion, drug utilization (antiplatelet agents, heparin bridge, non-steroid anti-inflammatory drugs (NSAIDs), and steroid), hemodialysis, CHADS2 score. The predictors of delayed bleeding were analyzed in a multivariate analysis by logistic regression model.
**Results:** A total 312 patients with gastric neoplasms were identified. The mean and median age of patients were 75.1 ± 7.8 and 76 (48–92), and male was 71.4%. Most neoplasms were located in gastric body (84.6%), and two-thirds of lesions were protruded type. The proportion of continuous antiplatelet agents, heparin bridge, NSAIDs, and steroid utilization were 8.4%, 9.2%, 3.2%, and 5.8%, respectively. Median glomerular filtration rate (GFR) was 61 (5–107), and 16 patients (5.1%) underwent hemodialysis. Delayed bleeding rate was 8.7% (27/312), and median onset of bleeding was post operation day 1 (1–16). Four patients (1.3%) encountered repeated delayed bleeding, and three of them received heparin bridge therapy. Median hospitalization was 8 days (7–24), which was significantly longer in heparin bridge cases. Delayed bleeding was associated with age (>75), lesion site (antrum), heparin bridge, hemodialysis, and CHADS2 score (>3) in a univariate analysis. A multivariate analysis showed CHADS2 score (>3) was an independent predictor of delayed bleeding after gastric ESD (Odds Ratio 3.14 [95%CI 1.17–8.22], p = 0.024).
**Conclusion:** CHADS2 score (>3) is a predictor of delayed bleeding after endoscopic submucosal dissection for gastric neoplasms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0431 DIAGNOSTIC SCORES AS PREDICTORS OF OUTCOME IN PATIENTS WITH BLEEDING PEPTIC ULCERS

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**Introduction:** The aim of this study was to compare Rockall score (RS), Baylor bleeding score (BBS) and Glasgow Blatchford score (GBS) in predicting clinical outcomes and the need for interventions in patients with bleeding peptic ulcers.
**Aims & Methods:** Between January 2008 and December 2013, 1012 consecutive hospitalized patients managed for peptic ulcer bleeding (PUB) were included into the study.For every patient we calculated preendoscopic (RS, BBS and GBS) as well as postendoscopic diagnostic scores (RS and BBS), according to urgent upper endoscopy findings. The area under the receiver-operating characteristics curve (AUROC) was calculated for predicting lethal outcome, rebleeding, predicting the need for blood transfusion and surgery.
**Results:** PUB made up 41.9% of all bleedings from upper gastrointestinal tract, 5.2% patients died and 5.4% patients underwent surgery. By comparing the AUROC curves of before mentioned preendoscopic scores, RS was the best score for predicting lethal outcome (AUROC 0.82 vs 0.67 vs 0.63, respectively). Postendoscopic RS was better than postendoscopic BBS in predicting lethal outcome in patients with peptic ulcer bleeding (AUROC 0.82 vs 0.69, resepectively). GBS was the best score in predicting rebleeding (AUROC 0.75 vs 0.61 vs 0.53, respectively), in the predicting of need for blood transfusion (AUROC 0.83 vs 0.63 vs 0.58, respectively) and surgery (0.82 vs 0.63 vs 0.52, resepectively) among this three pre-endoscopic scores.
**Conclusion:** In the group of patients with bleeding peptic ulcers RS was the best in predicting mortality, but GBS was the best in predicting rebleeding rate, in predicting the need for blood transfusion and surgery intervention.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Abstract No: P0429**

Risk of Upper gastrointestinal Bleeding of Current use of Ginkgo biloba.

| Time Window | Exposure periods (N = 1504) | Control periods (N = 1504) | Crude OR Point estimate | 95%CI | P |
|---|---|---|---|---|---|
| Total upper gastrointestinal bleeding | | | | | |
| 1-7 day window | 97 | 38 | 5.21 | 2.94-9.24 | <0.0001 |
| 1-14 day window | 111 | 69 | 2.45 | 1.59-3.77 | <0.0001 |
| 1-28 day window | 140 | 100 | 1.82 | 1.28-2.57 | 0.0008 |
| Severe bleeding in need of blood transfusion | | | | | |
| 1-7 day window | 62 | 21 | 7.83 | 3.35-18.32 | <0.0001 |
| 1-14 day window | 68 | 37 | 3.39 | 1.82-6.28 | 0.0001 |
| 1-28 day window | 81 | 60 | 1.78 | 1.11-2.85 | 0.0168 |

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## P0432 MANAGEMENT OF ACUTE UPPER GASTROINTESTINAL HAEMORRHAGE IN A DISTRICT HOSPITAL


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**Introduction:** Acute upper Gastrointestinal (GI) Bleeding is the commonest emergency managed by Gastroenterologists. Most deaths occur in elderly patients who have significant co-morbidity and the majority are inevitable, despite improvements in medical and surgical expertise. Mortality is reported to be lower in specialist units and this is probably not related to technical developments but because of adherence to protocols and guidelines.
**Aims & Methods:** The aim of this audit was to look into the compliance with the National Guidelines which were published by the Scottish Intercollegiate Guidelines Network (SIGN) in 2008. Information was gathered retrospectively on 50 patients admitted to a district general hospital with acute upper gastrointestinal haemorrhage.
**Results:** They were 16 females and 34 males with age range of 18–90 years. Data on the date and time of admission, using Rockall scoring system, time of referral to the gastroenterologist, restoring eth circulatory volume and the time of endoscopy were collected from the case notes. These data were analysed based on SIGN national standards in managing upper gastrointestinal bleeding. Results showed that 92% of the patients were admitted under non gastroenterologist physician as part of the on call take. Majority of patients (90%) was referred to the Gastroenterologist within the first 24 hours of admission. The severity of the bleeding was assessed in only 44% of the patients using Rockall scoring system. The circulatory volume was restored in all of the patients with intravenous fluids or blood transfusion. Not all of the patients (only 44%) had an endoscopy within 24 hours and there was no out of hours endoscopists on site unless the on call physician was a gastroenterologist.
**Conclusion:** The initial management of acute upper gastrointestinal bleeding is very important. In a district general hospital, the lack of out of hour endoscopists and the long waiting time for the endoscopy list may delay the appropriate timing of endoscopy. Our study showed that we need to train junior doctors how to use the Rockall scoring system. Following this audit, a standard Performa for clerking patients with upper gastrointestinal bleeding was developed. Regarding out of hour endoscopists cover, a proposal was put forward to provide funding to ensure that patients with bleeding would have endoscopy within 24 hours of admission.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0433 MEDICAL VERSUS ENDOSCOPIC TREATMENT OF OESOPHAGEAL VARICES IN LIVER CIRRHOSIS


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**Introduction:** Portal hypertension is the most common complication of liver cirrhosis. (1) It may be complicated by gastrointestinal bleeding from oesophageal or gastric varices. (2) Treatment of varices can be medical by using non-selective beta blockers (as propranolol or cavedilol), or endoscopic (endoscopic variceal ligation EVL, endoscopic injection sclerotherapy EIS), or both. (3).
**Aims & Methods:** This study was conducted on 80 patients with liver cirrhosis and oesophageal varices (O.V.) grade III and IV, who were classified into five groups. Group I, 20 patients were subjected to EVL alone, group II, 20 patients received carvedilol alone (6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week), group III received propranolol alone (20 mg three times daily), group IV, 20 patients who were subjected to EVL combined with carvidolol (6.25 mg once daily, then increased to 6.25 mg twice daily after 1 week) and group V, 20 patients who were subjected to EVL combined with propranolol (20 mg three times daily). All patients were followed up by doppler study of portal vein and upper G.I. endoscopy.
**Results:** Upper G.I. endoscopy was done for all patients every 3 months up to 12 months. In the 1st visit, 95% of group I patients had O.V. grade IV and 5% had grade III O.V., by the 4th visit 80% had O.V. grade I and 20% had no O.V. in the same group. In group II, in the 1st visit 90% of patients had O.V. grade IV and 10% had O.V. grade III, in the 4th visit 60% had O.V. grade I and 40% had no O.V., In group III, in the 1st visit 95% of patients had O.V. grade IV and 5% had O.V. grade III, in the 4th visit 50% had O.V. grade I and 30% had no O.V., In group IV, in the 1st visit 20% of patients had O.V. grade IV and 80% had O.V. grade III, in the 4th visit 40% had O.V. grade I and 60% had no O.V., regarding group V, in the 1st visit, 75% had grade IV O.V. and 5% had O.V. grade III, while in the 4th visit 60% had O.V. grade I and 40% had no varices.
**Conclusion:** The combination of carvedilol and EVL is more effective in treating medium and large sized O.V. than EVL alone or EVL combined to propranolol.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0434 PERFORMANCE OF THE GLASGOW BLATCHFORD SCORE IN UPPER GASTROINTESTINAL BLEEDING: FOR WHICH PATIENTS, FOR WHAT OUTCOME AND WITH WHICH THRESHOLD?


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**Introduction:** Acute upper gastrointestinal bleeding (UGIB) is the most common medical emergency managed by gastroenterologists. It accounts for 5% of presentations to the emergency department (ED) and 2% to 3% of hospital admissions. Overall mortality remains around 8%[1]. Several practice guidelines and risk scores, combining clinical and endoscopic parameters, have been developed to predict the outcomes of these patients. Their aim is to assist physicians in the early stages of decision making. In 2000, Blatchford developed a clinical score that predicts the need for treatment in acute UGIB[2]. The score ranges from 0 to 23 and the risk of requiring treatment increases with increasing score. Patients presenting to the ED with UGIB and a GBS score of 0 have been shown to be safe for discharge and can be managed in an outpatient setting. However, patients are routinely hospitalized.
**Aims & Methods:** We retrospectively studied all patients presenting to the emergency department with upper gastrointestinal bleeding over 3 years. We defined UGIB as hematemesis, melena, and/or rectal bleeding, the latest only if it was accompanied by anemia (haemoglobin $< 10$ g/dl) and/or syncope. Primary outcome was the need for clinical intervention: blood transfusion, endoscopic, radiological or surgical intervention. We assessed the accuracy of the Glasgow Blatchford scoring system by plotting its receiver-operating characteristic (ROC) curve.
**Results:** We included 257 patients in final analysis. A total of 50.2% patients received one or more transfusion with packed red blood cells, fresh-frozen plasma and/or platelet concentrates. Sixty three (24.5%) patients underwent endoscopic hemostasis. Six patients (2.3%) underwent emergency surgery and 7 (2.7%) received interventional radiology. Mean GBS was 9.4 ($\pm$4.1). No patient who needed clinical intervention (blood transfusion, endoscopic, surgical, or radiologic management) was not identified by the GBS. The area under ROC curve reaches 92.3%. Thirty nine (15.2%) patients had a GBS $\leq 4$. None of them needed intervention.
**Conclusion:** We validated the Glasgow Blatchford score in the setting of a Belgian university hospital. Given its high sensitivity, it is probably the safest scoring system to predict the need for treatment of patients presenting to the emergency department with symptoms of acute upper gastrointestinal bleeding. To reduce unnecessary admissions, a cut-off value of $\leq 4$ can be used safely and effectively in our institution as it predicts the need for clinical intervention with 100% sensitivity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0435 APPROACH OF REBLEEDING IN UPPER GASTROINTESTINAL NON-VARICEAL HAEMORRHAGE

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**Introduction:** Upper gastrointestinal bleeding (UGIB) represents a common and challenging emergency for gastroenterologists. The morbidity and mortality of upper GI bleeding remains high in patients with recurrent bleeding or significant co-morbid illnesses.
**Aims & Methods:** Aim The aim of this study is to assess the factors associated with rebleeding rate in upper GI non variceal haemorrhage especially: the aetiology, presence of comorbidities, type of treatment and final outcome. Methods We have performed a retrospective analysis of the patients admitted with upper GI non-variceal haemorrhage and rebleeding between 2014–2016 in Clinical Emergency Hospital Bucharest. We have used resuscitation methods at presentation, blood transfusions, intravenous PPI, endoscopic hemostasis and surgical treatment when needed.
**Results:** We had in total 1600 cases of upper GI non-variceal haemorrhage with 71 cases of recurrence. The mean age of the patients was 60. Also, 84.5% of the patients with rebleeding presented comorbidities. The mean value of Rockall score was 6. The causes of rebleedings were represented by: duodenal ulcers in 34% of cases (size over 1 cm, active bleeding, visible vessels), gastric ulcers 17%, anastomotic ulcers 16%, Dieulafoy's lesions 13%, duodenal angiodysplasia 4%, tumors 8%, Mallory Weiss lesions 4%, esophageal ulcers 3% and post sphincterotomy 1%. The type of endoscopic hemostasis used was combined in the majority of cases: injection, bipolar coagulation and hemoclips and successful in 84.6% of the cases. The average of repeated endoscopic hemostatic procedures was 3 but the highest number (4) was represented for Dieulafoy's lesion. Surgery was required in the rest of the cases (15.4%) for giant gastric ulcers, tumors, penetrating duodenal ulcers and spurting Dieulafoy's lesions. We had a mortality of 14% for the rebleeding group, most of them because of comorbidities and only 2 cases due to postoperative complications.
**Conclusion:** Repeated endoscopic hemostatic therapy for recurrent upper GI non-variceal bleeding (after successful initial endoscopic control of haemorrhage) represents the optimal choice with favourable results (84.6%). Patients at high risk, with increased value of Rockall score should be closely monitored for rebleeding. Multidisciplinary care, including endoscopists, surgeons, anaesthesiologists represents the best approach of upper GI non-variceal bleeding especially for recurrences.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0436 AMBULATORY HIGH RESOLUTION OESOPHAGEAL MANOMETRY: A NOVEL TOOL TO INVESTIGATE NONCARDIAC CHEST PAIN

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**Introduction:** Non-cardiac chest pain can present a clinical challenge to the gastroenterologist. Many causes remain undiagnosed and untreated.
Oesophageal spasm is frequently considered a cause of non-cardiac chest pain, but current diagnostic tools are often poor at making this diagnosis. High resolution oesophageal manometry is now the gold standard oesophageal motility test, and is a swallow-based assessment. Unfortunately most episodes of chest pain in this context are not swallowrelated, and are usually sporadic and unpredictable. Thus most manometry assessments occur in the absence of a symptom event.
We propose that prolonged, ambulatory high resolution may be a tool that can detect these sporadic chest pain events and allow correlation to symptom episodes.
**Aims & Methods:** We aimed to test the diagnostic yield of a novel, ambulatory high resolution oesophageal manometry device in the diagnosis of non-cardiac chest pain. We studied 17 patients (7 male, 10 female, age range 14 to 66) with chest pain. All had cardiac pain excluded by cardiology review, and all had been studied with normal upper GI endoscopy. All had also had major oesophageal motor disorder (including spasm) excluded by swallow-based high resolution manometry (with liquid and solid swallows). An ultra-thin high resolution solid-state catheter (Unisensor) was inserted transnasally into the oesophagus. This was connected to a small laptop and battery pack carried in a backpack (recording device an software, MMS). Patients were sent home and encouraged to mobilise. Patients were asked to keep the catheter in place at least until a symptomatic pain event was perceived. Symptom events were self-marked on a recorder device that was subsequently synchronised with the manometry output. Manometry tracings were read manually, and motor events at the time of symptoms were examined in detail.
**Results:** The median duration of recording with the system was 12 hours, 13 minutes (range 5 hours, 30 minutes to 26 hours, 40 minutes). 12 of the 17 patients perceived typical chest pain symptom during recording. Of the 12 with typical symptoms, 3 (25%) had clinically important findings that changed management. They had significant oesophageal spasm, pressurisation and shortening associated with pain events. These have been treated successfully with oesophageal body Botox injections (2 patients) and with long laparoscopic myotomy (1 patient). The remaining 9 patients either had no abnormalities, or minor abnormalities that did not correspond to symptoms.
**Conclusion:** Ambulatory high-resolution manometry is a novel tool for investigation of non-cardiac chest pain. In our series, we identified management-altering abnormalities in 3 of 17 (18%) patients who had previously been investigated with normal cardiac, endoscopic and stationary manometric evaluation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0437 HETEROGENEITY IN HIGH RESOLUTION MANOMETRY (HRM) AND AMBULATORY PH TESTING AROUND THE WORLD IN 2015

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**Introduction:** Despite advances in HRM and pH monitoring there is wide variation in technique and technology while reporting is often subjective and open to interpretation. This study assesses current practice around the world.
**Aims & Methods:** Through an on-line platform (Qualtrics LLC), a survey was distributed to unselected oesophageal units through international NGM societies. Questions explored infrastructure, technology, analysis and reporting. Results are presented as % of the total or mean ± SD.
**Results:** 91 of 102 responses from 29 countries were analysable (Table). 43 High (HVC) and 48 Low Volume Centres (LVC) were defined as more and less than 500 referrals/year. HVC employ more staff than LVC ($p = 0.02$) with more clinicians ($3.0 \pm 1.0$ vs. $2.6 \pm 1.2$; $p = 0.05$), physiologists ($1.6 \pm 1.1$ vs. $2.0 \pm 1.3$; $p = 0.07$) and nurses ($3.3 \pm 1.2$ vs. $2.4 \pm 1.1$; $p < 0.001$). Most units (63/91;69%) stop medication. 18 (20%) use $<12$ sensor manometry, 75 (82%) $>26$ sensor HRM and 53 (58%) use HRM-Impedance (some had several systems). Adjunctive testing is increasingly incorporated (Table). To define pathology, Chicago Classification is used in 65 (71%) units. 60% comment on the upper sphincter. In the presence of a hiatus hernia analysis of oesophago-gastric junction morphology varies widely (p = NS). 64% proceed with pH-monitoring despite ≥Grade B oesophagitis. If intolerant of the catheter, 45% refer for catheter-free monitoring and 16.5% for barium; 14% do nothing further. HVC are more likely to employ catheter-free systems than LVC (47% vs. 17%; $p < 0.001$). Of 86 (95%) units with Impedance-pH (Imp-pH), studies are performed on acid suppression in 54% with oesophagitis/Barrett's. Overall, 8% perform all Imp-pH studies on therapy, 9% never do. Dietary modification (acid avoidance) is always recommended in 48%. Meals/snacks are not analysed in 91% units with standard pH and 84% with Imp-pH. Overall 17% do not exclude meals with either. 75% manually analyse every Imp-reflux event while 59% only target symptoms. For symptom-association, 30% units pool symptoms while 74% analyse each separately. Therapy advice is included in 49% HVC and 31% LVC ($p = 0.044$); 40% overall.

| | Adjunctive Tests | Single Solid/ Viscous | Multiple water | Meal | Upright-seated swallows |
|---|---|---|---|---|---|
| Europe (n = 45) | 43 (96%) | 31 (69%) | 38 (42%) | 11 (24%) | 18 (40%) |
| USA (n = 14) | 10 (71%) | 6 (43%) | 7 (50%) | 3 (21%) | 6 (43%) |
| S. America (n = 8) | 9 (100%) | 5 (56%) | 7 (78%) | 0 (0%) | 5 (56%) |
| Australia/NZ (n = 12) | 11 (92%) | 10 (83%) | 8 (67%) | 2 (17%) | 6 (50%) |
| Asia (n = 5) | 6 (100%) | 3 (50%) | 6 (100%) | 1 (17%) | 2 (33%) |
| Africa/Middle East (n = 6) | 5 (100%) | 2 (40%) | 4 (80%) | 0 (0%) | 1 (20%) |
| Total (n = 91) | 84 (92%) | 57 (63%) | 70 (77%) | 16 (18%) | 38 (42%) |

**Conclusion:** There is marked heterogeneity in methodology, interpretation and presentation of HRM and pH studies around the world. This survey sets the background from which agreement of standard operating procedures can begin.
**Disclosure of Interest:** R. Sweis: Symposium funded by Given Img.
All other authors have declared no conflicts of interest.

## P0438 ENDOSCOPIC MYOTOMY FOR ACHALASIA USING THE HOOK KNIFE FOR A PRECISE CIRCULAR MUSCLE CUT: EVALUATION OF THE SAFETY AND THE EFFECTIVENESS OF THE 132 FIRST CASES

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**Introduction:** Per oral endoscopic myotomy (POEM) is an emerging minimally invasive procedure for the treatment of achalasia. However the precise technique can be refined and the hook knife can be used to precise the myotomy. We evaluated its results in the 132 first patients of our institution.

**Aims & Methods:** All consecutive cases referred for POEM using the Hook Knife for the myotomy were included. The database was completed prospectively. Clinical evaluation (Eckardt score) was realized before the procedure and after procedure at 3 and 12 months. All patients underwent high-resolution manometry (HRM) before procedure and 3 months later to classify achalasia according to Chicago classification.

**Results:** 132 patients (75 men, mean age 53 years) were included. Typical achalasia represented 117 cases (type I :13, II: 81, III :23), Jackhammer esophagus 1 case, and it was not possible to pass the manometry cathter through the esophago-gastric junction (EGJ) in 13 patients. Ninety one patients did not receive any previous treatment, 23 underwent pneumatic dilation, 12 Heller myotomy, 2 botulinum toxin injection and pneumatic dilation, 1 botulinum toxin injection alone and 3 patients a previous POEM. Procedure was incomplete in 8/134 (6%) cases: 3 for several submucosal fibrosis, 2 for mucosal injury of the tunnel in the cardia, 1 for diverticulum on the tunnel way, 1 for peptic ulceration and 1 for food stasis (success during the second attempt two weeks later). Procedures were complete in 126 other cases (93.9%). Dual Knife ® (n = 115) or the water jet Nestis Enki 2 ® (n = 11) were used for the tunnel. No mucosal injury was observed with the water-jet system. Hook Knife ® was used for all the myotomies and allowed a precise circular myotomy. The average time of procedure was 76.1 min with a clear learning curve (155–23 min). A pneumoperitoneum was exsufflated with a needle during the procedure in 70 cases (53.1%), we noticed subcutaneous emphysema in 39 (29.5%) cases, without any visible perforation. The 23 first patients were explored by systematic CT scan at day 1 with a pneumomediastinum (n = 20/23), a pneumoperitoneum (n = 20/23) and/or a pneumothorax (n = 7/23). Two (1.5%) patients presented a hematoma of the tunnel, diagnosed with pain and aphagia, one at day 1 and the other at day 5 without any other bleeding. Those hematoma were treated conservatively. No sepsis was observed. Feeding was always possible with liquids at day 1. Nine patients were discharged at day 1 without any further adverse events. All patients noted a clinical improvement. Three months after POEM (available for 87 patients) mean Eckardt score was 1.3 (0–7) versus 7.2 (3–12) before ($p < 0.001$). The EGJ resting pressure significantly decreased (7.9 mmHg (0–39) versus 26.8 mmHg (2–81) before POEM, $p < 0.001$) as well as integrated relaxation pressure (7.8 mmHg (0–24) versus 23.7 mmHg (3–79) before POEM, $p = < 0.001$).

**Conclusion:** Myotomy with hook knife is very precise, safe and effective. Only 2 hematoma of the tunnel were observed on the 134 cases. Due to the low rate of adverse events, we now recommend a discharge at the day after the myotomy; CT scan is no longer peformed systematically but only in case of symptoms.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0439 ENDOSCOPIC PYLOROMYOTOMY VIA GASTRIC SUBMUCOSAL TUNNEL DISSECTION: A PROMISING TECHNIQUE FOR GASTROPARESIS

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**Introduction:** Pyloroplasty has been the most common treatment for the pyloric diseases. But it is still associated with complication of leakage, post-operational stenosis and general anesthesia. Therefore, the development of minimally invasive but reliable method is highly desired. Inspired by the peroral endoscopic myotomy to treat achalasia, the novel technique of endoscopic pyloromyotomy has been designed. The aim of this study is to investigate the feasibility and efficacy of endoscopic pyloromyotomy via gastric submucosal tunnel dissection.

**Aims & Methods:** The 5 pigs were studied for the procedure. The pyloromyotomy via the submucosal tunnel dissection was performed as the follows: (1) the incision site of mucosa was defined on the posterior gastric antral wall 5cm proximal to the pylorus; (2) saline solution mixed with norepinephrine and methylene blue was topically injected for submucosal lifting; (3) 1-2cm mucosal incision in longitudinal length was made to create the submucosal tunnel entry; (4) The submucosal layer was carefully disassociated until pyloric muscular layer was identified; (5) 1-2cm pyloromyotomy were performed; (6) After endoscope withdrawal, mucosal defect were closed with clips. Pigs were euthanized and necropsies were performed.

**Results:** Dissection of pylorus muscle was successful in the pigs. Bleeding was limited during the procedure. No complication of perforation was observed.

**Conclusion:** The endoscopic gastric submucosal tunnel dissection technique was feasible and effective for pyloromyotomy. It is also easy to perform and minimally invasive for clinical application. Further studies need to perform for confirming the safety and efficacy on the human, and the clinical advantages other than traditional techniques.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0440 OPTIMAL NUMBER OF MULTIPLE RAPID SWALLOWING DURING HIGH RESOLUTION OESOPHAGEAL MANOMETRY

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**Introduction:** Low volume (10 ml) multiple rapid swallowing (MRS) has been proposed as additional test during oesophageal high resolution manometry (HRM) in order to assess pathophysiological alterations of clinical relevance. Generally one sequence is performed, however we have recently shown[1] that it is not reliable regarding presence of the after contraction and its strength.

**Aims & Methods:** To determine the optimal number of MRS in order to assess the peristaltic function. This is an interim analysis of an ongoing study. Thirty-five consecutive patients who underwent HRM were prospectively enrolled. Twenty-two had normal motility and 13 had ineffective esophageal motility (IEM) diagnosed according to Chicago 3 classification. The HRM protocol consisted in: five single five ml swallows (SS), five MRS followed by another five SS and five MRS. Measures were as follows: a) highest value of DCI (DCImax) during SS and MRS respectively, b) number of SS and MRS needed to detect DCImax, c) minimum number of MRS needed to detect MRS/SS DCI ratio > 1 (i.e. peristaltic reserve), d) minimum number of MRS needed to detect DCI > 450 mmHg.s.cm. in severe IEM (patients where all SS had a DCI < 450 mmHg.s.cm). Chi squared test and Wilcoxon test were used when appropriate.

**Results:**

| | All patients | IEM (13) | Normal motility (22) | P value * |
|---|---|---|---|---|
| Number of SS to detect DCImax | 5; 1–10 | 7; 2–10 | 5; 1–8 | 0.03 |
| Number of MRS to detect DCImax | 4; 1–10 | 4; 2–6 | 4.5; 1–10 | 0.5 |
| Number of MRS to detect MRS/SS DCI ratio > 1 | 1; 1–4 | 1; 1–4 | 1; 1–4 | 0.81 |

Data expressed as median; $10^{th}$–$90^{th}$.* IEM vs normal motility Results, median ($10^{th}$ to $90^{th}$ percentile), see table: In IEM patients DCImax during MRS was higher than during SS (1098; 657–1760 vs 741; 399–930; $p = 0.019$) whereas it was not different in patients with normal motility (2439; 1886–5002 vs 2302; 1719–5231); $p = 0.36$). A highly variable number of sequences of both MRS and SS were needed in order to identify DCImax. 12/13 IEM and 14/22 normal motility patients had a peristaltic reserve, which was detected within three and four sequences of MRS respectively ($90^{th}$ percentile). The first MRS sequence detected peristaltic reserve in seven IEM and nine normal motility patients, that is only 58% and 64% of all patients with peristaltic reserve in both groups. Patients who had severe IEM (5/13) reached a DCI > 450 mmHg.sec.cm with the first MRS (3/5) or never (2/5).

**Conclusion:** In a cohort of patients with oesophageal symptoms the number of MRS needed to reach DCImax was quite variable, however peristaltic reserve was reliably detected within three to four MRS sequences and ability to produce an effective wave (DCI > 450) in severe IEM was detected at the first MRS sequence. Our data suggest that four MRS sequences should always be performed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### Reference

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## P0441 MOTILITY AND OESOPHAGEAL CLEARANCE IN BARRETT'S OESOPHAGUS

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**Introduction:** It is not clear if Barrett's is a consequence of excessive reflux only or reduced clearance of refluxed materials. This study compares oesophageal reflux over 24 hours and High Resolution Manometry (HRM) response to solids in Barrett's with non-Barrett's reflux (NBR).
**Aims & Methods:** Reports for 19 consecutive patients (M58:F14) with ≥2 cm Barrett's during 2015 were compared with 25 patients with NBR (M10:F16) and 22 patient controls with normal physiology/endoscopy (M6:F16). All had at least one typical symptom of heartburn, regurgitation or chest pain. All had HRM with the intention of completing 10 × 5cc water and 5 × 1cc bread. Contractile vigour was measured with the Distal Contractile Integral (amplitude x length x contraction time); DCI > 450 mmHg.cm.s and breaks in peristalsis of < 5 cm were considered the lower limit of normal contraction as per Chicago Classification 3.0. Standard reflux and impedance parameters were assessed. 11/19 Barrett's were on while all NBR were off treatment.
**Results:** Lower oesophageal sphincter pressure was lower in Barrett's (8 vs. 14 mmHg; p = 0.009). Compared to NBR, patients with Barrett's (2–10 cm) had significantly reduced DCI for both 5 ml water (318 vs. 650 mmHg.cm.s; p = 0.007) and solid (1096 vs. 2002 mmHg.cm.s; p = 0.009). On the other hand, the likelihood of measuring a DCI of > 450 was significantly reduced in Barrett's only with solids (69% vs. 100%; p < 0.001) not water (32% vs. 54%; p = 0.224). Peristaltic effectiveness based on HRM was also reduced only for solids (44% vs. 65%; p = 0.029). All reflux parameters were similar between the two groups: total (p = 0.116), upright (p = 0.233) and supine reflux (p = 0.110), symptom index (p = 0.16), symptom association probability (p = 0.106) and total number of reflux events (p = 0.063). On the other hand, bolus clearance time (BCT) was significantly prolonged for Barrett's (13 vs. 10 s; p = 0.009) solely due to prolonged supine BCT (14 vs. 10 s; p < 0.003). Bolus exposure time (BET) was significantly prolonged for Barrett's (p = 0.011) due to both daytime (4.49% vs. 1.73%; p = 0.015) and nocturnal BET (0.75% vs. 0.24%; p = 0.002). Comparing those with prior endoscopic Barrett's therapy (n = 6) with treatment naïve (n = 13), there was no difference in any motility or pH monitoring parameter apart from BET which was greater in those who received therapy (5.87% vs. 1.99%; p = 0.046).
**Conclusion:** Solids were superior to water swallows in demonstrating ineffective contractility in Barrett's. This was associated with reduced nocturnal oesophageal clearance and increased exposure to refluxate during the day/night. These findings contribute to the theory of impaired contractility and reduced clearance despite acid-reducing medication in Barrett's.
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## P0442 STUDIES OF THE CLINICAL DIAGNOSTIC VALUE OF THE ESOPHAGEAL HYPERTENSIVE PERISTALSIS BASED ON QUESTIONNAIRE, ESOPHAGEAL RADIOGRAPHY AND HIGH RESOLUTION MANOMETRY

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**Introduction:** According to the Chicago criteria version3, patients with esophageal hypertensive peristalsis of DCI between 5000 to 8000 mmHg.s.cm were definite as "normal". However, many of such patients presented symptoms such as dysphagia, chest pain, et al.
**Aims & Methods: Aims**: To compare the clinical symptoms, esophagography and esophageal motility characteristics between Jackhammer esophagus and other esophageal hypertensive peristalsis, and to analyze the clinical diagnose value of patients with EHP.
**Methods**: All patients underwent esophageal manometry were screened from Jan1st 2012 to Apr 1st 2015. The patients with esophageal hypertensive peristalsis were enrolled in the study. All enrolled subjects underwent esophageal radiography. Part of the patients fulfilled the dysphagia questionnaire. We defined the hypertensive peristalsis area (HPA) as an area in 180 mmHg isobaric contour. The patients with HPA but not reaching the Jackhammer criteria were defined as other esophageal hypertensive patients (OEHP). The data were analyzed by SPSS17.0 software.
**Results:** sixty-four in 543 patients (11.8%) were found to have HPA. Among them, 15.63% were Jackhammer esophagus, and 67.2% were OEHP patients. Esophageal radiography showed 5 patients presented esophageal spasm in 10 Jackhammer, and 30.2% (13/43) OEHP patients showed esophageal spasm. No statistical differences were found between these two groups (P > 0.05). There were no significant differences in the symptoms, esophageal forms and LES functions between Jackhammer esophagus and OEHP patients (p > 0.05), except the peristalsis amplitude. The dysphagia questionnaire investigations were completed in 34 patients. There were negative correlations between solid food dysphagia frequency and esophageal DCI, the esophageal peristaltic amplitude 3 cm above LES, the esophageal peristaltic amplitude 3–7 cm above LES (r = −0.445, P = 0.008, r = −0.354) P = 0.040, r = −0.459, P = 0.006). Negative correlations were found between solid food dysphagia extent score and average DCI, amplitude 3–7 cm above LES (r = −0.349, P = 0.043; r = −0.400, P = 0.019).
**Conclusion:** (1) Patients with HPA were not uncommon. (2) Jackhammer esophagus and OEHP were considered to be two subgroups of a spectrum. It's valuable to give the OEHP a definite diagnosis and recommended for further treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0443 DOES BALLOON DILATATION AFFECT PER-ORAL ENDOSCOPIC MYOTOMY PROCEDURE?

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**Introduction:** Per oral endoscopic myotomy (POEM) is a minimally invasive endoscopic treatment option for achalasia patients. The aim of the study is to evaluate whether previous history of failed balloon dilatation has any effect over POEM procedure in our clinic.
**Aims & Methods:** Between May 2014 and March 2016, 140 patients with achalasia who were naïve or previously endoscopically treated with pneumatic balloon dilatation underwent POEM. 134 of these patients with control endoscopy and high resolution manometry results were included into the trial. The procedure was carried out at the endoscopy unite in the gastroenterology clinic under general anesthesia by an endoscopist who was experienced at endoscopic submucosal dissection (ESD) and was educated for POEM. All POEM procedures were done with a triangle knife. Demographic data was recorded before the procedure and results of the procedure were recorded prospectively. Data of POEM procedure and demographics were compared between the balloon dilatation (BD) and naïve groups.
**Results:** 47 patients in BD group and 87 patients in Naïve group underwent POEM. There was no statistical difference between the groups regarding age, gender, tunnel and myotomy lengths, preoperative and postoperative Eckardt scores, total times of the procedure, rate of complications (p > 0.05). The median age of the patients was 42 (12–73) years. Preoperative and postoperative median Eckardt scores were 8 (5–12) and 0 (0–2) respectively. The median total time of the procedure was 52 (27–153) minutes, tunnel length 17 (12–27) cm and myotomy length was 14 (9–25) cm. Postoperative oral intake started at median 1 (1–2) day and length of stay was 5 (3–7) days. Capnoperitoneum developed during the procedure in 53 (39.4%) patients and was treated with veress needle. Mucosal perforation developed in 2 patients and was treated with endoscopic hemoclips successfully. 30 patients had esophagitis (26 Grade A, 3 Grade B, 1 Grade C) at control endoscopy in third month after the procedure.
**Conclusion:** We think that previous history of failed balloon dilatation in achalasia does not affect POEM procedure performed by an endoscopist experienced in advanced endoscopic techniques such as ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0444 ESOPHAGEAL SHORTENING IN HIGH RESOLUTION MANOMETRY: DOES IT MEAN ANYTHING?

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**Introduction:** Esophageal shortening is an occasional finding on HRM secondary to longitudinal muscle contraction. Fluoroscopy and magnetic field associated to HRM established physiological shortening in 1.8 cm. It is not known whether > 2 cms oesophageal shortening has clinical relevance.
**Aims & Methods:** Patients with ≥ 2 cm shortening anytime during a HRM (MMS water perfused 22 channels) were identified between 454 consecutive procedures between 2013 and march 2016. We evaluated the HRM following Chicago v.3 criteria. Symptoms, demographic and manometric patters (included multiple swallows test) were compared with patients without shortening.
**Results:** 33 (7.3%) patients with ≥ 2 cm shortening were identified between 454 HRM. 11 (33%) of shortening group were male, not finding differences with control group (41%). 51.5% (17) of shortening group had "normal" HRMs and 4 patients had a Minor Peristaltic Disorder (Ineffective Esophageal Peristalsis). 5 patients had Achalasia diagnosis (4 type II and 1 type III). 3 were diagnosed of EGJ obstruction, 2 patients were diagnosed of Distal Esophageal Spasm, two were diagnosed of Rumination Syndrome and another patient had Jackhammer esophagus. Comparing with non-shortening, Major Motility Disorders were significantly more frequent (p 0.003) in shortening patients. No statistical differences were found in symptom pattern regarding heartburn, regurgitation, abdominal pain, pharynx discomfort, chronic cough, halitosis, asthma and conditions such as Functional Dyspepsia or Irritable Bowel Syndrome. However dysphagia was more frequent in shortening patients (p

0.027). Regarding EGJ (esophageal gastric junction), no differences were found in manometric sub types I, II or III prevalence between both groups. 21 of shortening patients were studied by 24 h pH/impedance test, being 9 abnormal. No differences seem to be present with the non-shortening group (38% abnormal pH/impedance). Multiple swallow test was pathological more frequently in shortening group (p 0.0001).

**Conclusion:** A larger proportion of Motility Disorders were found in patients with $\geq$ 2 cm oesophageal shortening finding in HRM. No statistical differences were found in symptomatic patterns except for dysphagia, more frequent in shortening group. Multiple swallow test is also pathological more frequently in shortening patients, probably explained by a more prevalent dysphagia. Esophageal shortening is a phenomenon that can be found in normal HRM. However, its association with Motility Disorders invites to register this finding and to pay special attention in these patients follow up.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0445 MACROPHAGE FUNCTIONAL ACTIVITY DEPENDING ON THE REFLUXATE TYPE IN GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** Gastroesophageal reflux disease (GERD) is one of the most common clinical problems in daily practice and is associated with active mucosal inflammation including a moderate infiltration of macrophages in esophageal mucosa. The modern understanding of the cell and molecular pathogenesis of GERD-associated mucosal inflammation suggest a complex and multifactorial immune-mediated effects of the recurrent exposure of the esophagus to acidic and nonacidic refluxate of gastric contents (containing duodenal and intestinal proteases as well as acid and gastric pepsin) from the stomach.

**Aims & Methods: Aim**: to assess the change of macrophage activity inclusive of phenotype according to the refluxate type.

**Material and methods**: Macrophage phenotype activity was assessed in vitro by adding acidic and nonacidic refluxates of patients (n = 26) with different pH (4.6–6.6, n = 10; 6.7–7.2, n = 10; 7.3–8.1, n = 6) to peritoneal macrophages of C57/BL6 mice (n = 26) with the following macrophage culturing in standard conditions (10% FBS, RPMI1640) for 36 hours. Pooled analysis of macrophage phenotype included assessment of Th1/Th2 cytokine production in culture medium (Antigenix America, Mouse Th1/Th2/Th17 (18-Plex Panel)), typical M1/M2 surface macrophage CD markers (monoclonal antibodies CD25, CD80 and CD163, CD206, respectively) performed by flow cytometry (Beckman Coulter FC500).

**Results:** In groups of comparison with pH 4.6–6.6 and 6.7–7.2 analysis of cytokine production revealed the prevalence of Th1 inflammatory and Th1/Th2 bivalent cytokines production. The indices of Th1/Th2 summary cytokine production were 3.6 and 2.8, respectively. The most expressed changes were observed in the levels of IL1b, IL-8, IL-6 and TNF-a ($41.4 \pm 6.8$ vs $33.6 \pm 5.1$ pg/ml; $68.3 \pm 5.9$ vs $42.8 \pm 5.1$pg/ml; $75.4 \pm 6.9$ vs $52.1 \pm 5.6$ pg/ml; $23.5 \pm 1.8$ vs $18.7 \pm 1.6$ pg/ml, respectively; $p < 0.05$). In the group of pH 7.3–8.1 the index of Th1/Th2 cytokine production was 1.6, indicating the elevated concentrations of Th2 cytokines as compared to the other experimental groups. The most expressed changes were observed in IL-10: $27.7 \pm 2.6$ pg/ml in 7.3–8.1pH vs $16.2 \pm 1.8$ and $4.2 \pm 0.6$ pg/ml in 6.7–7.2 and 4.6–6.6 pH groups, respectively ($p < 0.05$). The expression of surface M1/M2 macrophage CD markers significantly varied. In 6.7–7.2 pH group the ratio of M1/M2 (CD25+CD80/CD163+CD206) CD markers expression was 1.9 and in 7.3–8.1 pH group M1/M2 index was 1.2.

**Conclusion:** Assessment of macrophage phenotype activity depending on pH of the GERD refluxate showed the prevalence of M1 (Th1) proinflammatory activated macrophages with increased expression of M1 surface markers (CD80, CD25) and predominantly increased production of Th1 cytokines (IL-1 b, IL-8, TNF-a) in the cells exposed to acid refluxate. The effect of mild-alkalotic refluxate also turned in M1 (Th1) macrophage phenotype but with the distinct trend of M2 (Th2) CD markers and Th2 cytokine production increasing as compared the other groups.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0446 IMPAIRED MUCOSAL INTEGRITY IS PRESENT IN SOME REFRACTORY GORD PATIENTS: THE RELEVANCE OF THE REFLUXATE

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**Introduction:** Clinical manifestations of gastro-oesophageal reflux disease (GORD) are known to result from prolonged contact of gastric acid with the oesophageal epithelium. It is commonly believed that the acidity of the refluxate is the major responsible agent altering tissue integrity and provoking symptoms. Nevertheless, over 30% of patients with GORD symptoms do not have pathological reflux. Based on the current pathophysiology we believe that oesophageal integrity plays an important role in symptom perception.

**Aims & Methods:** In this study we evaluated oesophageal mucosal integrity and its interaction with different reflux parameters in patients with typical GORD symptoms refractory to proton pump inhibitor (PPI) therapy. Twenty nine patients with typical refractory GORD symptoms, off PPI treatment during 2 weeks and 20 healthy volunteers (HV) were included in the study. Endoscopy and 24 h multichannel-intraluminal impedance (MII-pH) measurements were performed in both groups. Oesophageal biopsies were collected 3–5 cm above the lower oesophageal sphincter and mounted in Ussing chambers to evaluate transepithelial electrical resistance (TEER) and passage of fluorescein (Fl) in vitro. After the endoscopy, a MII-pH catheter was placed transnasally and 24 h recordings were performed to investigate the following reflux parameters: acid exposure (% time), total number of reflux events, number of acid and non-acid reflux events and total volume exposure. Furthermore, symptom association probability (SAP) and Symptom Index (SI) were calculated. These parameters were correlated with TEER and passage values. Data are presented as mean±SD and were analyzed using t-tests, a p-value $< 0.05$ was considered statistically significant.

**Results:** Based on SAP and SI scores our cohort consisted of 7 true GORD, 6 hypersensitive and 13 functional heartburn patients. A substantial overlap and variability was found in TEER and passage values both in HV and patients. A significantly lower TEER ($182.8 \pm 79.$ 6 Ωxcm$^2$ vs $238.1 \pm 70.2$ Ωxcm$^2$, $p = 0.0069$) and higher passage ($57.01 \pm 9.3$ pmols vs $21.83 \pm 3.4$ pmols, $p = 0.0022$) was found in GORD patients compared to HV. Despite the differences in permeability measures, no correlations between oesophageal integrity (TEER and passage) and reflux parameters of interest could be found (Table 1). Based on the 95$^{th}$ percentile, subgroups of patients with normal and hyper-permeability were made. Increased permeability to Fl was found in 14/29 GORD patients. However, in these subgroups no differences were found between reflux parameters. The proportion of patients with a positive SAP and/or SI was similar in the normo- and hyperpermeability subgroups.

**Table 1:** Correlation between TEER and passage and reflux parameters in refractory GERD patients off PPI.

| | Acid exposure (% time) | Total nr of reflux | Nr of acid reflux | Nr of non-acid reflux | Total volume exposure (% time) |
|---|---|---|---|---|---|
| **TEER** | | | | | |
| r-value | 0.000305 | −0.2566 | −0.1558 | −0.2443 | −0.07 |
| p-value | 0.9988 | 0.1964 | 0.4376 | 0.2195 | 0.717 |
| **Passage** | | | | | |
| r-value | −0.2151 | 0.0992 | −0.03183 | 0.301 | −0.06 |
| p-value | 0.2913 | 0.6297 | 0.8773 | 0.1351 | 0.763 |

**Conclusion:** Despite the impaired integrity found in refractory GORD patients, none of the reflux parameters were associated with oesophageal integrity, and this was the case both in patients with normo- and hyperpermeability. The lack of association with acid reflux and other reflux parameters strongly suggest that other factors besides number and acidity of reflux events may play an important role in the pathophysiology of refractory GORD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0447 DUODENAL EOSINOPHILIA AND POSTBRANDIAL DISTRESS SYNDROME ARE ASSOCIATED WITH AN INCREASED RISK OF NEW ONSET GASTROESOPHAGEAL REFLUX IN FUNCTIONAL DYSPEPSIA: PROSPECTIVE TEN YEAR FOLLOW-UP OF THE KALIXANDA STUDY

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**Introduction:** Functional dyspepsia (FD) and gastroesophageal reflux disease (GERD) overlap more than expected by chance. One subtype of FD, postprandial distress syndrome (PDS) has been linked to impaired fundic accommodation which potentially can induce increased transient lower esophageal sphincter relaxations and GERD. Also, duodenal eosinophilia has been linked to functional dyspepsia (FD).[1, 2] However, the link between FD and GERD is not fully understood.

**Aims & Methods:** Our aim was to identify if there is an association between duodenal eosinophilia and FD, the subtypes of postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS) (Rome III definition) and new onset gastroesophageal reflux symptoms (GERS) in a population-based follow-up study. We also evaluated whether baseline GERS is linked to new onset FD. Methods: 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 esophagogastroduodenoscopy in 1999–2001. All eligible from the endoscoped cohort (n = 887) were invited to a follow-up study in 2010 with the ASQ. In a subsample of 175 subjects, eosinophil counts by histology[1] from the duodenum were evaluated at baseline. Data were analyzed by chi square test, Fishers exact test and logistic regression.

**Results:** Of 887 subjects at follow-up, in total 703 (79.3%) completed the questionnaire. FD was reported by 110 subjects (15.6%) at baseline (87 PDS and 35 EPS, overlap in 12) and by 93 (13.3%) at follow-up (79 PDS and 21 EPS, overlap in 7); overlap in 45 between baseline and follow-up; in total 158 subjects with FD. GERS without organic disease was reported by 185 subjects (26.3%) at baseline and by 203 subjects (28.9%) at follow-up (overlap in 128); in total 260 subjects, of whom 77 had developed new onset GERS at follow-up. PDS with no overlapping GERS (n = 34) at baseline was associated with new GERS at follow-up (13/77 vs. 21/626, $p < 0.001$, OR 5.66, 95% CI 2.68–11.98), but EPS (also without overlapping GERS, n = 13) was not (3/77 vs. 10/626, p = 0.16, OR 2.50, 95% CI 0.66–9.49), Table. Of the 127 subjects with baseline eosinophil counts from the duodenum, FD was reported by 29 subjects (22.8%, 95% CI 15.4–30.2) at baseline (24 PDS and 10 EPS, overlap in 5) and by 22 (17.3%, 95% CI 10.4–24.0) at follow-up (20 PDS and 3 EPS, overlap in 1); overlap in 10 between baseline and follow-up (41 subjects with FD). GERS (no organic disease) was reported by 19 subjects (16.2%, 95% CI 9.5–23.0) at baseline and by 36 subjects (30.8%, 95% CI 22.3–39.2) at follow-up (overlap in 14); 41 subjects, of whom 22 had developed new onset GERS at follow-up. Change from PDS with no overlapping GERS (n = 16) at baseline to new onset GERS at follow-up (8/22 vs. 8/105, p = 0.001) was associated with duodenal eosinophilia, OR 17.96; 95% CI 2.0 – 161.4, but EPS (n = 8, 3/22 vs. 5/105, p = 0.14) was not, OR 0.6; 95% CI 0.05 – 7.53. In contrast, baseline GERS without baseline FD was not associated with new onset FD (2/22 vs. 9/105, p = 1.0).

PDS at baseline and new onset reflux at 10 years, Age categorized at 60 years, PPI use during the last 3 months, *H. pylori* positive on culture/histology (n = 703)

| | OR | 95% CI |
|---|---|---|
| New onset reflux at 10 years | 5.66 | 2.68–11.98 |
| Gender | 1.04 | 0.50–2.18 |
| Age | 0.80 | 0.38–1.68 |
| PPI | 2.95 | 0.93–9.38 |
| *H. pylori* | 1.05 | 0.48–2.33 |
| Alcohol > 100 g/week | 0.55 | 0.12–2.43 |
| Smoking | 1.56 | 0.66–3.70 |

**Conclusion:** Duodenal eosinophilia is associated with an 18-fold increased risk of new onset GERS at 10 year follow-up in those with FD and PDS at baseline but not EPS. PDS but not EPS has been linked to gastric disaccommodation[3]. Duodenal eosinophilia may thus explain the link between GERD and FD via impaired gastric accommodation and increased transient lower esophageal sphincter relaxations[3], suggesting FD and GERD are part of the same disease spectrum. Our novel hypothesis that duodenal eosinophilia impairs gastric accommodation and predisposes to GERD is further supported by the fact that baseline GERS was not associated with new onset FD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0448 ESOPHAGO-GASTRIC JUNCTION MORPHOLOGY VARIABILITY DURING STANDARD MANOMETRIC PROTOCOL AND AFTER ESOPHAGEAL STIMULATION AND BODY CHANGE POSITION

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**Introduction:** High-resolution manometry (HRM) provides a better representation of the esophagogastric junction (EGJ) isolating the crural diaphragm (CD) from the lower esophageal sphincter (LES). According to the Chicago Classification (CC), three different EGJ subtypes can be detected based on the separation between the LES and the CD. However, few concerns have been raised about the possibility to describe a dynamic structure like the EGJ by a single snapshot taken at the beginning of the test.

**Aims & Methods:** We aimed to assess whether EGJ morphology may vary during the standard manometric protocol and after esophageal stimulation and body change position. Consecutive patients with esophageal symptoms presenting to different motility laboratories in Italy were enrolled. Patients underwent upper endoscopy off-therapy and solid state HRM with the following protocol: 5-min baseline recording after probe introduction, 10 single water swallows (WS, 5 mL), 2 multiple rapid swallows (MRS, five 2 mL water swallows 2–3 s apart), change of body position (seated) and multiple water swallow (MWS, 200 mL of water using 'multiple rapid swallows' without stopping). Tracings were analyzed based on CC vers. 3 and EGJ morphology was assessed after each step as: Type I, no separation between the LES and the CD; Type II, > 1 and < 2 cm of separation; Type III, > 2 cm of separation. In case of reflux symptoms, patients also underwent pH (-impedance) testing off-therapy [abnormal if acid exposure time higher than 4.2% or number of reflux episodes greater than 54 or positive symptom-reflux association using symptom association probability (SAP+ if ≥ 95%) and symptom index (SI+ if ≥50%)].

**Results:** We enrolled 89 [52M/37 F; mean age 52 (18–82); mean BMI 25 (17–35)] outpatients. Based on CC, we identified 50 (56%) patients with EGJ Type I, 18 (20%) with EGJ Type II and 6 (7%) with EGJ Type III, in whom no EGJ changes occurred during standard manometric protocol or after esophageal stimulation or body change position. In contrast, we identified 15 (17%) patients in whom EGJ morphology varied after WS (n = 6), MRS (n = 3), body change position (n = 4) or MWS (n = 4). In particular, in 2 patients there was more than one change. All patients with EGJ variation who underwent pH- (impedance) monitoring had an abnormal test (7/9, 78%), whereas this phenomenon occurred only in 13 out of 34 (38%) patients with stable EGJ (p = 0.0591). Endoscopy did not vary between the two groups [abnormal in 4/15 (33%) with changed EGJ vs. 13/74 (18%) with stable EGJ, p = 0.1745].

**Conclusion:** Esophago-gastric junction morphology varies only in a minority of patients, suggesting that the single assessment at the beginning of the test has a high per patient reproducibility. On the other hand, EGJ changes occurring during HRM testing are associated with more objective evidence of GERD, thus confirming the major role of EGJ as anti-reflux barrier.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0449 INCREASED INTRA-BOLUS PRESSURE IS MORE COMMON IN PATIENTS WITH NON-CARDIAC CHEST PAIN THAN IN THOSE WITH HEARTBURN – A STUDY USING HIGH-RESOLUTION MANOMETRY

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**Introduction:** The aetiology of Non-Cardiac Chest Pain (NCCP) is poorly known and different factors including esophageal motility abnormalities have been implicated. However, previous studies with conventional manometry failed to observe specific monometric features associated to NCCP. Indeed, hypercontractility of the esophageal body or rapid propagation of peristaltic wave were also common in asymptomatic subjects. High Resolution Manometry (HRM) is actually considered the ''gold standard'' to assess esophageal peristalsis and esophago-gastric junction (EGJ) function. Based on this technology, novel metrics have been developed to define esophageal motility abnormalities. Limited data are available in patients with NCCP.

**Aims & Methods:** We aimed to investigate whether patients with NCCP and reflux-related heartburn (RH) present different HRM features. We included consecutive patients with NCCP or RH as stand-alone symptom, referring to our motility laboratory. Patients with gastro-intestinal surgery, achalasia or scleroderma were excluded. Heartburn was considered reflux-related in case of complete symptom relief after at least 8 weeks of anti-secretory therapy. All patients underwent esophagogastroduodenoscopy off-antisecretory drugs (discontinued at least 30 days before the endoscopy) to assess the presence of esophageal mucosal lesions and HRM with 5-min baseline recording and 10 single water swallows. The diagnostic criteria for manometry agreed with the Chicago Classification vers. 3. Further, a normal IBP was defined in case of a mean value lower than 17 mmHg and therefore abnormal in case of a mean value $\geq$ than 17 mmHg. Data were expressed as mean and standard deviation.

**Results:** Between March 2014 and March 2015, we included 24 patients (9 Male/15 Female, $56 \pm 15$ years) with NCCP and 47 patients ($50 \pm 13$ years; 19 M/28F) with RH. No differences were found in terms of age, sex and BMI between the two groups ($p = ns$). Patients with NCCP had a mean IBP higher than patients with RH ($18.6 \pm 6.7$ vs. $14.1 \pm 4.7$; $p = 0.02$) and had more frequently an abnormal IBP value (13 vs. 11; $p = 0.0161$). On the other hand, mean DCI ($4148 \pm 18598$ vs. $1563 \pm 1083$; $p = 0.6$) and IRP ($7 \pm 8$ vs. $4 \pm 6$; $p = 0.06$) were similar between NCCP and RH, respectively. Also no differences were found in terms of mean distal latency, mean contractile front velocity, frequency of different manometric patterns and EGJ morphologies ($p = ns$). Only 1/24 patients (4%) of the NCCP patients had endoscopic evidence of GERD, whereas in the RH group the number of patients with erosive esophagitis was higher (13/47; 28%; $p = 0.02$).

**Conclusion:** IBP is the only HRM metric that differed between patients with NCCP and those with RH suggesting that NCCP elicitation could be more associated to abnormal EGJ compliance (i.e. abnormal bolus transit and EGJ dysfunction) rather than abnormal vigor of peristalsis or contractile velocity.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0450 PREVALENCE RATE OF TYPE OF GASTROESOPHAGEAL JUNCTION IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD) AND PATIENTS WITHOUT GERD

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**Introduction:** High Resolution Manometry (HRM) allows to identify the different morphology of the esophagogastric junction (EGJ). In type EGJ I, diaphragm and lower esophageal sphincter (LES) conform a single pressure peak. Both EGJ II and III have a double pressure peak. In EGJ type II there is a separation lower than 2cms between diaphragm and LES, and in EGJ type III the separation is larger than 2cms (hiatal hernia). Hiatal hernia is traditionally associated with GERD.

**Aims & Methods:** Aims To assess the prevalence of each subtype of EGJ in GERD and non-GERD patients. Methods Descriptive retrospective study of 296 patients who underwent HRM and 24 h pH/impedance test. GERD was diagnosed by endoscopic findings or 24 h pH/impedance results. Separate prevalence of each EGJ subtype was compared in GERD vs non-GERD. Also double pressive peak EGJ (type II and III) was compared versus EGJ type I prevalence.

**Results:** Of 296 patients, 38.04% (112) were diagnosed GERD. In this group, 33% had EGJ type I, 38.4% EGJ type II and 28.6% EGJ type III. In non-GERD patients (61.95%, n:184), EGJ subtypes prevalence was EGJ I 49.5%, EGJ II 30.4% and EGJ III 20.1%. Globally, EGJ I is observed in 33% patients with GERD and 45.9% in non-GERD, reaching significant difference (p 0.02). EGJ II is most frequent in patients with GERD (38.4% vs 30.4%) as well as EGJ type III (28.6% vs 20.1%) but with no statistical differences. Grouping double peak morphology (EGJ II and III) it is observed that in GERD patients, EGJ I is found in 33% of cases, compared to 67% of patients with double peak. In non-GERD patients, the percentage of EGJ I is 49.5% vs 50.5% double peak EGJ. Proportionally, the single pressive peak respect the double pressive peak appears with a proportion 1:2 in patients with GERD, and with a proportion 1:1 in patients without GERD, with statistical significance ($p = 0.006$).

| | | EGJ I | EGJ II | EGJ III |
|---|---|---|---|---|
| GERD | n: 112 (38.04%) | 33% | 38.4% | 28.6% |
| Non-GERD | n: 184 (61.95%) | 49.5% | 30.4% | 20.1% |
| | | EGJ I | EGJ II+III | |
| GERD | n: 112 (38.04%) | 33% | 67% | |
| Non-GERD | n: 184 (61.95%) | 49.5% | 50.5% | |

**Conclusion:** The prevalence of the different types of GEJ significantly varies depending on the existence of GERD, with lower presence of EGJ I in patients with GERD.
If we assess the different types of EGJ separately, GERD patients do not present more frequently EGJ type II and there is non-significant trend towards EGJ III morphology.
Gastroesophageal junctions formed by double pressive peak (EGJ II and III) are more prevalent than single pressive peak in patients with GERD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0451 RELATIONSHIP BETWEEN GASTRIC ACCOMMODATION AND POSTPRANDIAL TRANSIENT LOWER OESOPHAGEAL SPHINCTER RELAXATIONS AND REFLUX EVENTS IN HEALTH AND GASTRO-OESOPHAGEAL REFLUX DISEASE/FUNCTIONAL DYSPEPSIA OVERLAP

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**Introduction:** Several studies reported a high symptomatic overlap between gastro-oesophageal reflux disease (GORD) and functional dyspepsia (FD). Impaired gastric accommodation (GA) is a well-established mechanism underlying symptom generation in FD and has been suggested to provide a plausible mechanism of overlap between GORD and FD.

**Aims & Methods:** Our aim was to study the relationship between GA, transient lower oesophageal sphincter relaxations (TLOSRs) and reflux events in healthy volunteers (HV) and patients with overlapping GORD and FD symptoms. Twenty HV (10 m, 23 y (range 19–36)) with no prior history of digestive disease and 10 patients with overlapping GORD and FD symptoms (2 m, 33 y (range 20–54)) underwent combined high resolution impedance and manometry (HRiM) monitoring, with the catheter (Unisensor AG, Attikon, Switzerland) placed into the stomach. Recordings were made 30 min before and 60 min after a high carbohydrate and high fat solid meal consisting of meatloaf, mashed potatoes and apple sauce (1000 kcal). Medical Measurement System (MMS, Enschede, The Netherlands) software was used for analysis. TLESRs and reflux events were identified and quantified using established criteria. In sensors 5 cm below the lower border of the lower oesophageal sphincter (LOS), the intra-gastric pressure (IGP) before, during and after the meal was measured. Area Under the Curve (AUC) of IGP during the meal, representing GA, was calculated. The relationship between GA, TLOSRs and reflux events was analyzed using Pearson and Spearman correlation tests.

**Results:** Seven of the 10 patients had pathological reflux on ambulatory 24-h ph-impedance monitoring. During meal intake, a small drop and subsequent rise in IGP was observed, both in HV and patients, with a bigger drop ($-1.79$ mmHg vs. $-2.47$; $p = 0.041$) and a lower rise (4.68 mmHg vs. 3.53 mmHg; $p = 0.068$) in patients. 60% of patients vs. 15% of HV did not complete the meal. No difference in the number of postprandial TLOSRs (10 (8–13) vs. 9 (5–12); $p = 0.666$) and associated liquid (2 (0–5) vs. 2 (0–6); $p = 0.838$), gas (1 (0–3) vs. 0 (0–5); $p = 0.869$) or mixed (0 (0–1) vs. 0 (0–1); $p = 0.283$) reflux events could be found between HV and patients. In HV, a significant positive correlation was found between the recovery of IGP during the meal, calculated as the slope from the minimum to the maximum IGP during the meal, and the total number of postprandial TLOSRs (Pearson $r = 0.49$; $p = 0.029$). This slope was lower in patients (0.69 vs. 0.50; $p = 0.058$). Also in HV, AUC of IGP during the meal tended to be correlated to the total number of postprandial TLOSRs (Pearson $r = 0.38$; $p = 0.097$) and the total number of postprandial TLOSRs associated with liquid reflux (Spearman $r = 0.40$; $p = 0.082$). These correlations were not found in the GORD/FD overlap patient group.

**Conclusion:** These findings confirm GA as a potential determinant of TLOSR and reflux occurrence in HV. In the present cohort of GORD/FD overlap patients, no significant correlation was found, suggesting involvement of other triggering pathways. Future studies will address differences in GORD/FD overlap patients with or without pathological reflux exposure as well as pure GORD patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0452 ACID SENSING ION CHANNELS AS TARGETS FOR THE MODULATION OF PAIN SENSATIONS IN GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** We earlier demonstrated that STW5 and omeprazole affect multiple chemokine families on genome and proteome level and involve G-protein coupled receptor and MAP-kinase signaling to reduce inflammation in the esophageal tissue in our rat model for gastro-esophageal reflux disease (GERD)[1]. We further reported a simultaneous upregulation of acid sensing ion channels (ASICs), especially ASIC4 and 5-hydroxytryptamin receptor (5-HTR) subtypes in the inflamed esophageal tissue and postulated both receptor types may form a communication network involved in pain signaling[2]. Chen and Wong[3] pointed out that ASICs alone are not sufficient to reconstruct the path of pain signaling. Evidence that ASICs are mechanically sensitive needs to be provided. Proteins proposed to be involved as mechanotransducers along with ASICs include extracellular matrix (ECM) proteins (collagens), ECM-linker proteins (matrilin-2), intra-cellular linker proteins (e.g. stomatin) and cytoskeleton proteins (actin filament, microtubule)[3].
**Aims & Methods:** We analysed in our subacut GERD rat model the transcript modulation of matrilin-2, stomatin and tubulin in the esophageal tissue.
**Methods**: Rats were pretreated with either STW5 (0.5 or 2 ml/kg), a multicomponent herbal preparation, or Omeprazole (O) (30 mg/kg). Esophagitis was induced surgically followed by a further 10 d treatment. On day 10 animals were sacrificed. RNA was isolated from defined tissue areas of the esophagi for Agilent whole genome microarray (rat). Data were analysed by Ingenuity[1].
**Results:** Tissues of animals suffering from GERD showed a small, but significant increase in the expression of stomatin (3.1f,) and of tubulin 6 (2.6f) ($p < 0.0001$) compared to ''normal'' tissue. Other tubulins or matrilin-2 were not regulated. In tissues of animals treated with either STW5 (2 ml/kg) or with O (30 mg/kg) stomatin (−4.8f; −2.6f) as well as tubulin 6 (−2.8f; −2.1f) were downregulated ($p < 0.0001$) by both treatments. The magnitude of regulation corresponded with the one of ASIC4[2].
**Conclusion:** Even though we did not yet investigate the identified molecules in function, data further support our hypothesis that a central pain response in peripheral nerve tissues is activated via ASICs in the presence or absence of acidic reflux and is positively influenced by STW5 and O.
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H. Abdel-Aziz: H. Abdel-Aziz received financial support for research from Steigerwald Arzneimittelwerke GmbH and joined Steigerwald Arzneimittelwerke GmbH, Bayer Consumer Health as employee.

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## P0453 RELEVANCE OF SLEEP DISTURBANCE TO THE INTEGRITY AND CHARACTERISTICS OF SECONDARY PERISTALSIS IN PATIENTS WITH GERD

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**Introduction:** Sleep disturbance is common in patients with gastroesophageal reflux disease (GERD). Secondary peristalsis is important for clearance of the refluxate from the esophagus.
**Aims & Methods:** We aimed to test the hypothesis that altered physiological characteristics of secondary peristalsis may occur in a subset of GERD patients with sleep disturbance and such alteration also correlated with the severity of sleep disturbance. Secondary peristalsis was performed with slow and rapid air injections into mid-esophagus in 8 age-matched health controls and 41 patients with GERD. Sleep disturbance was assessed by the Pittsburg Sleep Quality Index (PSQI) with >5 indicating sleep disturbance. Objective sleep measures were assessed by ambulatory actigraphy. We aimed to test the hypothesis that altered physiological characteristics of secondary peristalsis may occur in a subset of GERD patients with sleep disturbance and such alteration also correlated with the severity of sleep disturbance.
**Results:** The patient group included twenty patients with sleep disturbance and 21 patients without sleep disturbance. The threshold volume for inducing secondary peristalsis during slow air injection was significantly greater in GERD patients with sleep disturbance than healthy controls ($14.3 \pm 1.2$ vs. $8.9 \pm 0.5$ ml, $p < 0.05$). GERD patients with sleep disturbance had greater threshold volume of secondary peristalsis during rapid air injection than GERD patients without sleep disturbance ($5.1 \pm 0.4$ vs. $3.9 \pm 0.2$ ml, $p < 0.05$) and healthy controls ($5.1 \pm 0.4$ vs. $3.6 \pm 0.2$ ml, $p < 0.05$). The frequency of peristaltic response during rapid air injection was also significantly lower in GERD patients with sleep disturbance as compared with GERD patients without sleep disturbance (50% [22.5–67.5%] vs. 60% [50–90%], $p < 0.05$) and healthy controls (50% [22.5–67.5%] vs. 95% [72.5–100%], $p < 0.05$). There was a negative correlation between PSQI and peristaltic frequency during rapid air injection ($r = -0.39$, $p = 0.01$). Secondary peristaltic amplitude during rapid air injection was negatively correlated with wake after sleep onset ($r = -0.34$, $p = 0.04$).
**Conclusion:** Sleep disturbance is associated with attenuated mechanosensitivity to distension-induced secondary peristalsis and impaired secondary peristaltic competence in patients with GERD. The demonstrated relationships between sleep measures and peristaltic parameters suggest that sleep disturabnce per se may impact the effectiveness of esophageal peristaltic reflex.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0454 INFLAMMATION MIGHT HAVE A ROLE IN EROSIVE ESOPHAGITIS BUT NOT IN NON-EROSIVE REFLUX DISEASE

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**Introduction:** The relationship between inflammatory activation mechanisms and acid-peptic injured esophageal tissue is not clear. We evaluated whether there are differences between inflammation and tight junctional proteins such as e-cadherine among subtypes of gastroesophageal reflux disease (GERD).
**Aims & Methods:** The aim of this study was to investigate any possible role of inflammation in pathologic mechanism of reflux disease by determining the inflammatory markers in injured esophageal tissue as well as serum of patients. Three groups (erosive-EE, n = 18; nonerosive-NERD, n = 12; healthy controls-HC, n = 13) were evaluated with high-resolution esophageal manometry, 24 h pH-intraesophageal impedance, upper gastrointestinal endoscopy and mucosal impedance measurements. The esophageal biopsies and blood samples were collected. Serum e-cadherine levels, NFkB, chitotirosidase (CHIT), myeloperoxidase (MPO) activities in serum and homogenized tissues were determined.
**Results:** NKFB levels in tissue was significantly higher in subjects with EE ($4.9 \pm 2.53$ ng/mg.prt) versus HC ($2.95 \pm 1.51$ ng/mg.prt, $p = 0.018$). MPO tissue activities in EE group were significantly lower ($0.07 \pm 0.06$ u/mg.prt) than HC ($0.23 \pm 0.22$ u/mg.prt, $p = 0.025$) while MPO serum levels were higher in EE ($1.15 \pm 1.63$ uL) versus HC ($0.56 \pm 0.69$ uL, $p = 0.045$). Tissue CHIT levels were three fold increased in EE versus HC ($p = 0.071$). None of these measurements showed any differences in NERD group. NFKB and MPO levels had a negative correlation ($r = -0.408$, $p = 0.005$) in tissue. NFKB and ECAD levels had a positive correlation in serum ($r = 0.642$, $p < 0.0001$). Mucosal impedance in EE ($1200.8 \pm 305.6$ ohms) was significantly higher than HC ($3956.7 \pm 1920.7$ ohms, $p = 0.001$) and also NERD ($2882.2 \pm 1296.0$ ohms, $p = 0.001$), while there were no significant differences between NERD and HC.
**Conclusion:** Inflammatory process might play a pivotal role in injured mechanism only in erosive esophagitis but not in NERD. The lower values of mucosal impedance measurements also support this assumption that impaired tissue integrity might be an outcome of inflammation in erosive esophagitis. Non-inflammatory mechanisms might be responsible such as hypersensitivity in patients with NERD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0455 TJ-14 (HANGESHASHINTO) IMPEDES THE DEVELOPMENT OF REFLUX-INDUCED ESOPHAGEAL CANCER IN A SURGICAL RAT MODEL

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**Introduction:** Hangeshashinto (TJ-14), a Japanese Kampo medicine, has been reported to be effective in preventing chemotherapy-induced oral mucositis through the reduction of prostaglandin E2 (PGE2). TJ-14 has also been shown to affect cyclooxygenase activity. M2 phenotype macrophages contribute to tumor development in the immunosuppressive microenvironment. Therefore, targeting the immunosuppressive network in tumor tissues, by inhibiting PGE2, may provide an effective preventive strategy. We evaluated the effectiveness of TJ-14 as a chemoprevention agent in a surgical rat reflux model of esophageal cancer.
**Aims & Methods:** The rat reflux model was created by performing an end-to-side esophagojejunostomy on Sprague Dawley rats. The surgery promoted the reflux of gastro-duodenal contents into the esophagus. The rats were divided into 2 groups. One group was given commercial chow (control group), and the other

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The Results

| | MPO (tissue) u/mg.prt | MPO (serum) uL | CHIT (tissue) nmol/mg.prt | CHIT (serum) ng/mL/h | NFkB (tissue) ng/mg.prt | NFkB (serum) nmol/mg.prt | Ecad (serum) ng/ml | Mucosal impedance (ohms) |
|---|---|---|---|---|---|---|---|---|
| EE (total) (n = 18) | **0.07** [a] | **1.15** [b] | 1.86 | 19.72 | 5.84 | 8.62 | 7.95 | **1200.8** [j,k] |
| NERD (n = 13) | 0.13 | **1.10** | **0.31** | **15.62** | **4.90** | **10.36** | **8.07** | **2882.2** |
| HC (n = 13) | **0.25** | **0.56** | **0.62** | **18.26** | **2.95** | **9.40** | **7.90** | **3956.7** |
| ERD-A (n = 6) | **0.09** | **0.66** | **1.13** | **8.54** | **3.16** | **9.08** | **6.46** | – |
| ERD-B (n = 8) | **0.08** [f] | **1.44** [d] | **3.11** | **32.93** [e] | **6.00** [c] | **6.26** | **7.36** | – |
| ERD-C (n = 4) | **0.03** [h] | **1.35** [i] | **1.39** | **10.09** | **5.32** [g] | **12.66** | **11.93** | – |

a: p = 0.025, b: p = 0.045, c: p = 0.01, d: p = 0.076, e: p = 0.013, f: p = 0.045, g: p = 0.023, h: p = 0.007, i: p = 0.057, j: p = 0.001 (vs. HC), k: p = 0.001 (vs. NERD)

was given experimental chow, containing TJ-14 (TJ-14 group). All surviving animals were sacrificed 40 weeks after surgery and their esophagi were examined. The primary antibodies against CD163 (M2; AbD Serotec) were used for immunohistochemistry.

**Results:** Twenty two rats survived 40 weeks post-surgery and were included in the study. Of these, 12 were included in the control group (Figure 1a), and the remaining 10 received TJ-14 administration (Figure 1b). 67% (8/12) of the controls developed esophageal cancer (Figure 1c), but animals that received TJ-14 had a cancer incidence of 10% (1/10) (p = 0.007, Chi-squared) (Table 1). Barrett's metaplasia was found in 83% (10/12) of the rats in the control group (Figure 1d). However, only 50% (5/10) of the rats in the TJ-14 group displayed signs of Barrett's metaplasia, indicating a protective tendency of TJ-14. All of the rats in the TJ-14 and control groups developed proliferative hyperplasia. M2 phenotype macrophage decreased in the TJ-14 group compared to the control group.

**Conclusion:** TJ-14 protected against the development of esophageal cancer in a clinically relevant surgical reflux model. Further investigation is required regarding the potential clinical use of TJ-14 as a chemopreventive agent.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0456 IN VITRO AND EX-VIVO QUANTITATIVE ASSESSMENT OF LOCAL INTERACTIONS OF ANTACIDS WITH OESOPHAGEAL MUCOSA FOCUSED ON LAYER STABILITY AND RESISTANCE TO HCL PENETRATION: SIGNIFICANT THERAPEUTIC IMPLICATIONS

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**Introduction:** Liquid formulations of antacids are widely used for the treatment of heartburn and some antacids e.g, hydrotalcite was shown to protect and heal ulcerated oesophageal mucosa. Hydrotalcite (HTL) is a "layer-lattice" antacid. The liquid formulation of HTL contains 1000 mg per dose. The formation of a stable layer on top of the mucous lining and its acid penetration resistance is thought to be crucial for the liquid formulation, however these properties have not been quantitatively assessed and tested. HTL protects the stomach and oesophageal mucosa and improves the quality of mucosal repair. Its protective properties have been documented in animal and human studies*.

**Aims & Methods:** The objective of the study is to characterise the action of HTL Liquid using physicochemical model systems and compare it with three other commercially available antacids: 1) another liquid layer-lattice antacid with 1600 mg magaldrate (ANT 1) per dose; 2) with a liquid algeldrate magnesium hydroxide mixture (ANT 2) and 3) with a combination of sodium alginate, sodium hydrogen carbonate and calcium carbonate (ANT 3). The mechanical stability of the liquid antacid formulations was tested on a de-wetting model experiment. As substrates standard glass plates and ex-vivo freshly excised porcine oesophageal mucosa were used. In this model the antacids form a layer on top of the substrate. The layers show different stability. Some of the antacids dewet the substrate which means they do not form a complete layer on it. This process occurs with the formation of small holes in the homogenous layer of antacids. As the background is dark, parts of the layers with different thickness have different colour intensity. The parts of the glass substrate which are dewetted are black in reflected light. The stability of the layers of antacids was defined as the time when the first de-wetting areas appear. The acid penetration resistance of a layer of antacid was defined as the time necessary for 0.1 M HCl to penetrate through a layer of antacid with defined thickness and area. The tests were performed in micro well plates (12 wells). The bottoms of the wells contained a thin layer of the pH sensitive indicator Pentamethoxy Red which is not soluble in the antacids. It is colourless at pH higher than 3 and red in the pH range below 3. The wells were filled with equal volumes of the tested antacids. On top of the antacids equal amounts of 0.1 M HCl was added. The change in the intensity of the red color of the samples was video imaged and quantified. The images were analysed using an Image J macro. The results were obtained from at least 5 separate tests.

**Results:** The acid penetration was after 40 minutes significantly longer (lower) for HTL than for ANT 2 and ANT 3 ($p < 0.001$ with ANOVA). The mechanical stability of the tested antacids showed that ANT 1 induced dewetting almost immediately after its application to the substrate whereas the other three antacids showed stable layers for at least 30 minutes. The results were similar on glass substrates and in ex-vivo porcine oesophageal mucosa. The acid penetration resistance for the chemical (acid neutralisation capacity) and physical (thickness and stability of the layer) resistance of an antacid layer were best for HTL and ANT 1. The stability of the antacid film however was the lowest for ANT 1.

**Conclusion:** 1) We established novel methods for the quantitative assessment of antacids interaction with oesophageal mucosa. 2) From four studied antacids HTL forms the most stable antacid layer both on glass substrate and on ex-vivo porcine oesophageal mucosa and has at the same time the best acid penetration resistance which might be of particular benefit in vivo.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0457 THE EXCRETION OF PANTOPRAZOL IN HUMAN BREAST MILK

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**Introduction:** Proton pump inhibitors are the most widely used medications and currently no data available about their concentrations in the human breast milk.

**Aims & Methods:** We aimed to measure the amount of pantoprazole in human milk after oral administration to a breast-feeding women and to estimate human exposure. Eight women who decided to stop breastfeeding were included. All subjects were taken 40 mg once a day of pantoprazole for 7 days. Blood and milk were collected at day 1 and 7 at 0–1.5–3–4.5–6–9–12$^{th}$ hours. A selective and rapid HPLC method was developed and validated for quantification of pantoprazol in plasma and breast milk samples using Omeprazol as internal standard. Pantoprazol was extracted from biological matrix by using Liquid-liquid extraction process. The method was validated over a linear concentration rage of 0.03–1 μg/mL and the limit of quantification (LLOQ) was 0.03 μg/mL.

**Results:** Pantoprazole was measured only in one sample of milk within 12 hours of period (7 measurements a day) at both days in all subjects. The mean concentration of pantoprazole was 54.8+24.1 (32.7–96.2) ng/ml for day 1 and 48.5+20.4 (21.7–82.9) ng/ml for day 7 in the milk. The detection of the drug in the milk was either at the time of the highest concentration of the blood or 90 minutes after the peak level. Eleven out of 16 detections in the milk were at the 3$^{rd}$ or 6$^{th}$ hour after administration of the drug.

**Conclusion:** The two compartment model was proposed to describe time profiles of pantoprazole in plasma and milk (plasma as central, milk as peripheral compartment). Pantoprazole's level of milk compartment was far less than plasma compartment. We estimate that 100 ml of milk contains about 50 mcg pantoprazole which means that the drug is minimally excreted. Since, pantoprazole is unstable in acidic pH, the systemic dose received by the infant might be even lower. Our limited data implicate that women who are breast-feeding might not stop breastfeeding when taking pantoprazole.

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## P0458 THE USE OF NON-ABLATIVE RF ENERGY (STRETTA) FOR THE TREATMENT OF GERD. TEN YEARS FOLLOW-UP RESULTS

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**Introduction:** To date, the Stretta procedure (Mederi Therapeutics Inc., Greenwich, CT, USA), which applies thermal radiofrequency energy to the LES, still remains an available technique for endoscopic treatment of GERD, with documented effectiveness on patient symptom control, quality of life (QoL), oesophageal acid exposure, and LES pressure. From June 2002 to March 2016 a cohort of 251 patients were consecutively treated with the Stretta procedure for GERD; 57 patients (36 females, 21 males) reached to date a ten year follow-up. Aim of the follow-up study is to verify durability, efficacy and safety of the procedure at this time.

**Aims & Methods:** Selection criteria for patients eligible to stretta were: hiatal hernia $<3$ cm, esophagitis not more than grade B, LES pressure not below 8 mmHg at preop manometric study, no dysmotility disorders of the esophageal body (except Ineffective Motility certainly secondary to GERD) and Barret's esophagus (except short segment BE). All patietns were under PPIs regimens, 26 out 57 of them still having ''extraesophageal'' symptoms as chronic cough, laringeal discomfort, dysphonia and nocturnal chest pain. All procedures were performed on an outpatient day-hospital basis; for deep sedation propofol (100–300 mg i.v.) and remifentanil (0.5–1 mg/kg/h i.v.) were administered with continue cardio-respiratory monitoring. The median procedure time was 40 minutes. Recovery mean time after procedure was 4, 5 hours and all patients were discharged from the hospital within the day. All patients received very detailed informations about dietary habits continued their current PPIs regimen for at least 0 days and then discontinued all antacid medications. All patients underwent to clinical interview after 6 months, 1 year, 4 years and ten years The primary outcomes of the study were heartburn (using a 6-point Likert scale ranging from no symptoms to incapacitating symptoms), GERD health-related quality of life (HRQL), using a 6-point Likert scale for multiple different symptoms, each ranging from no symptoms to incapacitating symptoms and general quality of life, using the medical outcomes 36-item Short-Form Health Survey (SF-36). GERD HRQL improvement was evaluated as a continuous variable and as a dichotomous variable (responder versus non-responder). A response was a $>50\%$ improvement compared with baseline values, as previously described.

**Results:** Out of 251 patients treated with Stretta from June 2002 to March 2016 a cohort of 178 did not reach at the date of the objective of a full 10 years follow-up, nine patients were lost to follow-up and in seven patients the RF treatment lost its efficacy. In all studied subjects there here was a significant decrease in both heartburn and GERD HRQL scores as well as a significant increase of QoL scores (mental SF-36 and physical SF-36). The Stretta procedure was very effective in patients suffering for extraesophageal symptoms, wich were resolved in 100% of them within the 6 months/one year controls. Forty-one patients out of 57 (71.9%) were completely off PPIs ten years after the Stretta procedure.

**Conclusion:** The Stretta procedure for GERD is now widely documented by experimental studies and clinical trials as effective and safe. The results of this follow-up study after 10 years confirms data published by Noar in late 2014 and further sustain the concept that Stretta might represent a viable treatment option for selected patients with symptomatic mild to moderate GERD; this suggestion has been recently stated by the SAGES Guidelines in 2013 and by the ASGE Guidelines in 2015. The Stretta RF treatment can be offered, especially to the younger GERD sufferers as a ''bridge therapy'' between the continuous medical treatment and the optimal timing for laparoscopic fundoplication and is indicated in refractory GERD and extraesophageal symptoms.

**Disclosure of Interest:** L. Dughera: I have received grants by mederi Therapeutics for training sessions.
All other authors have declared no conflicts of interest.

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## P0459 RESPONSE TO TREATMENT WITH PROTON PUMP INHIBITORS (PPI) OF ATYPICAL SYMPTOMS DEPENDING ON THEIR COEXISTENCE WITH TYPICAL SYMPTOMS

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**Introduction:** Gastroesophageal reflux disease (GERD) is divided according to the Montreal Classification into typical symptoms (heartburn and regurgitation) and atypical (cough, asthma and/or laryngitis). Response to treatment with proton pump inhibitors (PPI) suggests the relationship of these symptoms with GERD. It is unknown which factors could predict treatment response in these patients.

**Aims & Methods:** To study if the co-existence of typical and atypical symptoms is a predictive factor of PPI treatment response in atypical GERD-related symptoms. Observational retrospective study of 109 patients evaluated with 24 h pH/impedance test due to the presence of GERD typical and/or atypical symptoms. We evaluated the response to PPIs as indicated by their referring doctor. ''Response'' is defined as complete disappearance of symptoms and ''non-response'' if there is no improvement or if it is partial. Outcomes are compared between two groups: co-existence of Typical and Atypical symptoms and no co-existence (Atypical symptoms alone).

**Results:** Globally, in patients evaluated due to extra-esophageal symptoms (n: 109), symptomatic improvement with PPI treatment was found in 20.2% (20 patients) while 79.8% did not improve. Co-existence of typical and atypical symptoms of GERD was present in 66 patients and no co-existence in 43 patients. Evaluating the response to treatment, improvement was observed in 18 patients (18/66: 27.3%) in the co-existence group, while in patients with only atypical symptoms the improvement was detected in 4 patients (4/43: 9.3%). Regarding the global PPI response (n: 22), 18 ''co-existence'' patients improved (81.8%) versus 4 patients with atypical symptoms (18.2%).

| | | Non- PPI response | PPI response | Total |
|---|---|---|---|---|
| Atypical symptoms | N | 39 | 4 | 43 |
| | % | 90.7% | 9.3% | 100% |
| Atypical + Typical symptoms | N | 48 | 18 | 66 |
| | % | 72.7% | 27.3% | 100% |
| Total | N | 87 | 22 | 109 |
| | % | 79.8% | 20.2% | 100% |

**Conclusion:** 20.2% of patients evaluated due to extra-esophageal symptoms of GERD improved after PPI treatment. Treatment response was significantly larger in patients with coexistence (typical and atypical symptoms of GERD) versus 9.3% in patients with isolated atypical symptoms (27.3% vs 9.3%). The coexistence of atypical and typical GERD-related symptoms predicts a better response to treatment with PPIs of atypical symptoms compared to patients with isolated existence of atypical symptoms.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0460 A NEW GASTRIC ACID SUPPRESSOR, "VONOPRAZAN" IS EFFECTIVE IN PROTON PUMP INHIBITOR-REFRACTORY REFLUX ESOPHAGITIS

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**Introduction:** Proton pump inhibitors (PPIs) are the first choice of drugs for reflux esophagitis (RE). In 10–20% of patients with RE, there is incomplete healing of the mucosal injury even after a standard 8-week regimen of PPIs (i.e. PPI-refractory RE). Vonoprazan (VPZ) belongs to a new class of gastric acid-suppressing agents developed in Japan. It has potent and long-lasting anti-secretory effects on H+, and K+-ATPase owing to its high accumulation and slow clearance from the gastric tissue, resulting in a higher mucosal healing rate for patients with RE on initial therapy than in those receiving conventional PPIs (1–2). The purpose of this study was to elucidate the effect of VPZ using pH/impedance monitoring in patients with PPI-refractory RE.

**Aims & Methods:** All patients were tested for the cytochrome P450 (CYP) 2C19 genotype and *Helicobacter pylori* infection status at baseline, and were assessed using upper endoscopy, high-resolution manometry (Starlet, Star Medical, Inc., Tokyo, Japan), and pH/impedance monitoring (Sleuth, Sandhill Scientific, Highlands Ranch, CO. USA) after being on a standard PPI dose and 4 weeks after administration of VPZ (20 mg/day). The primary end-point of this study was the comparison of the percentage time to achieve intragastric and oesophageal pH $<4$ between patients on PPIs and on VPZ.

**Results:** Six patients with PPI-refractory RE (five women: mean age, 71.4 years; mean body mass index [BMI], 22.3, LA grade A/B/C/D, 1/1/2/2) were enrolled in this study. All patients were *H. pylori*- negative, and CYP2C19 extensive metabolizer, and had hiatal hernias. Four of the six patients achieved complete mucosal healing at 4 weeks. VPZ decreased the percentage time of the 24-h intragastric pH $<4$ significantly from 76.0 to 20.3% ($p=0.03$). Although VPZ decreased the percentage time of 24-h oesophageal pH $<4$ from 8.0 to 4.1%, but the difference was not significant ($p=0.42$). The acid clearance time significantly decreased from 352.6 to 115.8 s ($p=0.02$). The impedance study revealed a significant decrease in acid reflux events (19.2 vs. 6.0, $p=0.01$). However, significant differences were not found in the total reflux, non-acidic, proximal, and distal reflux events between patients on PPIs and those on VPZ (43.4 vs. 34.3, $p=0.11$; 21.6 vs. 28.2, $p=0.79$; 15.4 vs. 14.0, $p=0.08$; and 28.0 vs. 20.2, $p=0.11$, respectively).

**Conclusion:** VPZ significantly suppressed gastric acid secretion, and thereby, reduce the percentage time of the 24-h oesophageal pH $<4$, acid reflux events, and acid clearance time for patients on PPIs with PPI-refractory RE. Therefore, VPZ could be a potential optimal therapeutic strategy for patients with PPI-refractory RE.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0461 ENDOSCOPIC NON-ABLATIVE RADIO FREQUENCY ENERGY TREATMENT (STRETTA®) FOR GASTROOESOPHAGEAL REFLUX DISEASE – THE FIRST U.K. SINGLE-CENTRE EXPERIENCE

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**Introduction:** Gastro-oesophageal reflux disease (GORD) is usually treated with lifestyle modifications, combined with drug therapy (antacids, alginates and acid suppression drugs such as proton pump inhibitors and H2 receptor antagonists). Patients with inadequate response to lifestyle and medical treatments, or intolerant of medical therapy, are offered anti-reflux surgery with open or laparoscopic fundoplication which remains the gold standard[1, 2]. Stretta® is a minimally-invasive endoscopic treatment that delivers non-ablative radiofrequency (NARF) energy to improve and restore the function of the lower oesophageal sphincter muscle, thereby improving symptoms of GORD. The efficacy of the Stretta® procedure in achieving symptom control of GORD has been reported in previous international publications. A systematic review involving 20 studies with 1441 patients having a mean follow-up interval of 15 months showed significant improvements in GORD symptoms including disease-specific and global quality of life[3]. UK data on the outcomes of Stretta® have not been reported, and this is the first report of the Stretta® procedure in the UK, carried out at a single centre since October 2014.

**Aims & Methods:** Patients with confirmed GORD, unresponsive to medical management with standard or double dose PPI, were offered the Stretta® procedure based on clinician and patient shared decision. Patients with an associated hiatus hernia of $\leq$2 cm on their index endoscopy were included. Patients needed to be symptomatic of reflux for at least 3 months on medication and all patients were administered a GERD Health Related Quality of Life (GERD-HRQL) questionnaire pre and post-Stretta® procedure. The Stretta® procedure was carried out either under general anaesthesia (early phase) or conscious sedation (later phase) by a single trained endoscopist using the manufacturers protocol. Up to 14 lesion sets or 56 RF applications to the lower oesophageal sphincter at 1 cm intervals were carried out using an automated generator (Mederi Therapeutics Inc, USA).

**Results:** 26 patients underwent the Stretta procedure over a period of 12 months (October 2014 - September 2015). The mean follow-up period was 3.8 months (range 10.5) and there were no recorded procedural complications. All patients completed pre and post procedure GERD-HRQL questionnaires. The median heartburn score (scale 0–30) improved from18 pre-procedure to 2.5 post-procedure. The overall median regurgitation score (scale 0–30) improved from 19 pre-procedure to 0 post procedure. The overall patient satisfaction was 78%. There was also an improvement in the median overall total GERD-HRQL score (scale 0–75) from 44 pre-procedure to 6 post-procedure. 3 patients had undergone previous anti-reflux surgery. There was again overall improvement of median heartburn scores (18 pre, 0 post), regurgitation scores (1 pre, 0 post) and total GERD-HRQL scores (27 pre, 0 post). Baseline and post-procedure GERD-HRQL scores in 26 patients, average follow-up of 3.8 months:.

| Outcome variables | Pre-Stretta | Post-Stretta |
|---|---|---|
| Heartburn score | 18 | 2.5 |
| Regurgitation score | 19 | 0 |
| Patient satisfaction with GORD | 0% | 78% |
| Total GERD-HRQL score | 44 | 6 |

**Conclusion:** In this first UK report of Stretta, we demonstrate therapeutic benefit in medically non-responsive GORD, improving patient's heartburn, regurgitation and overall satisfaction scores with low procedural risks. There is also therapeutic benefit in patients with recurrent reflux symptoms after previous anti-reflux surgery, making it a possible treatment option for this group of patients. A larger UK Study is needed to incorporate Stretta into the therapeutic pathway for GORD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0462 THE CONCEIVED LIMITATIONS OF COMMONLY PRESCRIBED PROTON PUMP INHIBITORS IN THE TREATMENT OF GASTROINTESTINAL REFLUX DISEASE

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**Introduction:** Gastroesophageal reflux disease (GERD) is a worldwide highly prevalent disorder. Proton pump inhibitors (PPIs) have profoundly revolutionized the treatment of GERD. However, a substantial number of patients with GERD fail to respond adequately to PPIs. Available data on local attitudes and conceived limitations of treatment options for GERD among general practitioners (GP) and gastrointestinal specialists (GS) are scarce.

**Aims & Methods:** The aim of this study was to compare the common practices of family physicians and of GI specialists in the treatment of GERD, and to examine the conceived limitations of the available treatment options.

**Methods:** We conducted an internet survey addressed for GI specialist and family physicians during January to February 2016.

**Results:** 40 GS (18%) and 132 GP (10%) returned the questionnaire. Both groups treat 13–14 GERD patients/week (mean age 41–50 years). The most common indications for referral for a GI consultation were unresponsiveness to PPIs (46%) and presence of warning signs (weight loss, anemia, dysphagia, age $>$45 years, recurrent vomiting). GSs stated that the most important considerations for the selection of therapy were high safety profile; while GPs consider a rapid symptomatic relief. The most common first and second-line drug choices among both groups were omeprazole and esomeprazole, respectively. In the case of first and second line PPI failures, GSs tended to prescribe a non-PPI treatment, while GPs restarted esomeprazole. GSs stated that the commonest conceived limitations of PPI treatment were nighttime heartburn and undesirable side effects; while GPs considered treatment inflexibility (need to take on empty stomach before meals) and drug interactions. About 88% GSs and 55% of GPs would consider prescribing a new medication, if it would be long acting (covering the nighttime), prescribed once daily and without drug interactions.

**Conclusion:** GSs and GPs hold different attitudes to and conceive differently the limitations of the available PPI therapy. Despite these differences, it seems that PPI failure may be overcome by approaching two main unmet needs: nighttime heartburn and drug inflexibility.

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## P0463 HOW TO REDUCE THE FAILURE RATE OF NISSEN FUNDOPLICATION? A PILOT STUDY ON A NOVEL SURGICAL APPROACH FOR GERD TREATMENT

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**Introduction:** Laparoscopic Nissen fundoplication (NF) is considered the gold standard to treat gastroesophageal reflux disease (GERD) with a reported failure rate of 10–15%. In most cases, the wrap migration or disruption of hiatal repair represent the main cause of it.

**Aims & Methods:** We investigated whether a modified Nissen procedure (MNF) may reduce the failure rate of traditional Fundoplication. Between March 2011 and January 2016, we prospectively collected the clinical and pathophysiological data of consecutive GERD patients with typical symptoms who underwent MNF. Also, patients with prior surgical failure were enrolled. The surgical modification consisted of: 1) anchoring the esophagus to the diaphragmatic crura by means of two non-absorbable stitches on each side; 2) fixing the upper stitch of the valve to the diaphragm. In case of clearly weak crura, a reinforcement with dual mesh was used. Patients were evaluated before and after surgery with validated symptoms and quality of life (GERD-HRQL) questionnaires, upper endoscopy, barium-swallow, esophageal high-resolution manometry, and 24-hour impedance-pH monitoring. Surgical failure was defined in case of: (1) abnormal pH-Impedance; (2) esophagitis; (3) recurrence of hiatal hernia/slipped fundoplication; (4) persistence or early recurrence of GERD symptoms.

**Results:** Thirty-eight patients (20F/18M, mean age 56 $\pm$ 14 years) were included. Of them, 21 (55%) were refractory to PPIs, whereas 17 were on chronic treatment. In 9 cases (24%), MNF was performed as redo-surgery. The mean follow-up was 22 $\pm$ 10 months. In 28 patients surgery was completed laparoscopically;

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**Table 1:** Sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, positive predictive values, and negative predictive values of different combinations of DeMeester scroe, SI, and SAP for predicting response to treatment in patients with GORD.

| Test | Sensitivity (%) | Specificity (%) | Positive Likelihood Ratio | Negative Likelihood Ratio | Positive Predictive Value (%) | Negative Predictive Value (%) |
|---|---|---|---|---|---|---|
| abnormal DeMeester, SI +ve, OR SAP +ve | 80.00 (33.39–97.48) | 33.33 (11.82–61.62) | 1.20 (0.75–1.93) | 0.60 (0.14–2.51) | 44.44 (21.53–69.24) | 71.43 (29.04–96.33) |
| Abnormal DeMeester | 33.33 (7.49–70.7) | 87.50 (61.65–98.45) | 2.67 (0.54–13.10) | 0.76 (0.46–1.25) | 60.00 (14.66–94.73) | 70.00 (45.72–88.11) |
| SI +ve | 61.54 (31.58–86.14) | 58.33 (27.67–84.83) | 1.48 (0.67–3.27) | 0.66 (0.29–1.52) | 61.54 (31.58–86.14) | 58.33 (27.67–84.83) |
| SAP +ve | 77.78 (39.99–97.19) | 37.50 (15.20–64.57) | 1.24 (0.74–2.08) | 0.59 (0.15–2.35) | 41.18 (18.44–67.08) | 75.00 (34.91–96.81) |
| SI +ve AND SAP +ve | 66.67 (22.28–95.67) | 57.89 (33.50–79.75) | 1.58 (0.73–3.43) | 0.58 (0.17–1.90) | 33.33 (9.92–45.13) | 84.62 (54.55–98.08) |
| abnormal DeMeester AND SAP +ve | 60.00 (14.66–94.73) | 90.00 (68.30–98.77) | 6.00 (1.43–26.81) | 0.44 (0.15–1.31) | 60.00 (14.66–94.73) | 90.00 (68.30–98.77) |
| abnormal DeMeester AND SI +ve | 37.50 (8.52–75.51) | 93.75 (69.77–99.84) | 6.00 (0.74–48.90) | 0.67 (0.38–1.16) | 75.00 (19.51–99.37) | 75.00 (50.90–91.34) |
| abnormal DeMeester, SI +ve, AND SAP +ve | 60.00 (14.66–94.73) | 95.00 (75.13–99.87) | 12.00 (1.56–92.29) | 0.42 (0.14–1.24) | 75.00 (19.41–99.37) | 90.48 (69.62–98.83) |

conversion was necessary in 3 patients; 7 laparotomies ab initio. The median operating time was 157 ± 22 minutes. Mortality and post-operative complications were nil. All patients experienced complete symptom relief, but 2 did not improve due to dysphagia persistence (n = 1 redo) and severe dyspeptic symptoms (n = 1). Endoscopy was regular in all patients. After surgery, GERD-HRQL and symptom scores significantly decreased ($p < 0.001$), whereas pathophysiological findings significantly improved (Table).

| | **Before Surgery** | After Surgery | P value |
|---|---|---|---|
| Symptom score | 18 (14–21) | 0 (0–3) | $P < 0.001$ |
| Dysphagia score | 0 (0.5–1) | 0 (0–1) | $p = 0.88$ |
| GERD-HRQL score | 26.7 | 2.4 | $p < 0.001$ |
| LES resting pressure (mmHg) | 17.3 | 20.4 | $p = 0.67$ |
| LES residual pressure (mmHg) | 6.6 | 10.5 | $p = 0.50$ |
| LES total length (mm) | 3 | 3.3 | $p = 0.91$ |
| LES abdominal length (mm) | 0.7 | 1.5 | $p = 0.03$ |
| Acid exposure time (%) | 14.2 | 0.5 | $P < 0.001$ |
| Number reflux | 64.8 | 8.2 | $P < 0.001$ |
| Symptoms-reflux association (SI/SAP) | 16 pos | 0 pos | $P < 0.001$ |
| Antireflux medication | 17 (45%) | 2 (5%) | $P < 0.001$ |

**Conclusion:** Our data showed that the MNF was a safe and effective procedure, providing satisfactory clinical and pathophysiological outcome in the long-term (22 months), also in case of redo-surgery. In the end, in comparison to literature data, the failure rate also improved.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0464 CLINICAL YIELD OF USING COMMON REFLUX-SYMPTOM CORRELATION METHODS: A RETROSPECTIVE STUDY COMPARING THE DEMEESTER SCORE, SYMPTOM INDEX, AND SYMPTOMS ASSOCIATION PROBABILITY IN PREDICTING RESPONSE TO ANTIREFLUX TREATMENT IN PATIENTS WITH GORD

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**Introduction:** Oesophageal pH-impedance monitoring is the gold standard for the diagnosis of gastroesophageal reflux disease (GORD). The DeMeester score is calculated using different reflux parameters and serves as a global measure of acid exposure. Symptom Index (SI) and the Symptoms Association Probability (SAP) scores are also used to correlate symptoms to episodes of gastroesophageal reflux (GOR). Currently, it is not clear which of these scoring methods are best related to the patient's response to treatment. The aim of this study is to investigate the value of these 3 metrics in predicting the clinical outcome of treatment in GORD patients.

**Aims & Methods:** We retrospectively selected patients who had 24-hour pH-impedance monitoring on suspicion of GORD during December 2014 to October 2015. Abnormal DeMeester was defined as ≥ 14.72, +ve SI as ≥ 50%, and +ve SAP as ≥ 95%. The Reflux Disease Questionnaire (RDQ) was completed by each patient before investigation. After reflux monitoring was done, patients were followed up to calculate their post-treatment RDQ at least 2 months post treatment. Sensitivity, specificity, positive and negative likelihood ratios and predictive values were calculated.

**Results:** 42 patients (11 male; total mean age 51 [25–79]) were included. 25 (59.52%) of these patients were treated. Of these, 21 patients, had medical treatment and 6 had surgical treatment (2 had both). 10/25 (40%) had a reduced RDQ score post-treatment: 8/10 (80%) having medical treatment, 1/6 (23.33%) having surgical treatment. In patients without treatment, 7/17 (41.18%) had a reduced RDQ. The two-tailed p value between those treated and untreated group was not significant (P = 1.00). Considering individual metrics, abnormal DeMeester score showed highest specificity and SAP showed the highest sensitivity in predicting lowering RDQ score post-treatment. When combining different metrics, having all three parameters positive, yielded in the highest overall clinical value: Sensitivity 60%, specificity 95%, positive likelihood ratio 12, positive predictive value 75%, negative predictive value 90% (table 1).

**Conclusion:** In patients diagnosed with GORD by pH-impedance monitoring, having all three parameters positive i.e. abnormal DeMeester score, SAP +ve and SI +ve had a high overall value in predicting the response to treatment. Nevertheless, reduction of RDQ was equally seen in untreated GORD group. A study on a larger number of patients might be required to further confirm the findings of this research.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0465 A DOUBLE-BLIND, RANDOMIZED, MULTICENTER CLINICAL TRIAL INVESTIGATING THE EFFICACY AND SAFETY OF ESOMEPRAZOLE SINGLE THERAPY VERSUS MOSAPRIDE AND ESOMEPRAZOLE COMBINED THERAPY IN PATIENTS WITH EROSIVE REFLUX DISEASE

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**Introduction:** We aims to evaluate the efficacy and safety of combination therapy in ERD (erosive reflux disease) patients by comparing endoscopic healing rate according to the LA classification for esomeprazole alone and esomeprazole plus mosapride.

**Aims & Methods:** Patients complaining of reflux symptoms for the last 3 months and diagnosed with ERD according to the LA classification in an upper endoscopy were included in this study. A total of 116 patients were randomized to receive esomeprazole 40 mg once daily plus mosapride 5 mg three times daily (EM group), or esomeprazole plus placebo (E group) for 8 weeks. Patients recorded GERD symptom questionnaire at week 4 and 8. The primary endpoint was endoscopic healing rate of ERD after 8 weeks of treatment.

**Results:** The number patients showing improved endoscopic findings according to the LA classification was 32 (66.7%) in the EM group and 26 (60.5%) in the E group, but there was no statistically significant difference between the groups ($p = 0.692$). Only at 4 weeks, a total GERD symptom score changes relative to baseline significantly improved in EM group than that of E group (−13.4 ± 14.7

vs. $-8.0 \pm 12.3$, $p = 0.041$) and upper abdominal pain and belching score changes showed significantly improved in EM group than that of E group ($p = 0.018$ and $p = 0.013$, respectively).
**Conclusion:** The combination PPI with mosapride showed a tendency for upper abdominal pain, belching, and total GERD symptoms scores to improve more rapidly. This suggests that combination therapy with esomeprazole and mosapride will be useful for rapid improvement of symptoms in ERD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0466 ANTI-REFLUX ENDOSCOPIC SURGERY FOR REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** Currently, a variety of endoscopic procedures for gastroesophageal reflux disease (GERD) have been proposed. This suggests that anti-reflux endoscopic surgery (ARES) could achieve an effective anti-reflux procedure.
**Aims & Methods:** In this pilot study, 11 patients with refractory GERD received ARES, 3 of them has sliding hiatal hernia. ARES was crescentic conducted using cap assisted endoscopic mucosal resection method.
**Results:** Reflux symptoms of GERD improved significantly after ARES. In the GERD-Q score, mean score decreased from 13.8 to 5.8 ($P = 0.0001$). At endoscopic examination, the flap valve grade decreased from 3.2 to 1.2 ($p = 0.015$). Also the EGJ distensibility that was measured endoscopic.
**Conclusion:** This initial case series demonstrated the potential anti-reflux effect of ARES, with a crescentic mucosal resection appearing adequate. Further longitudinal study will be required to establish ARES as an effective technique to control GERD in this setting.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0467 ENDOSCOPIC TREATMENT VS. SURGERY FOR HIGH-RISK EARLY ESOPHAGEAL CANCER

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**Introduction:** Endoscopic treatment is a standard approach for patients with early esophageal cancer (EEC) with mucosal invasion (T1a). For patients with 'high-risk' T1a cancer (e.g. advanced grading or invasion to lymphatic vessels) and patients with any submucosal (sm) invasion (T1b), surgery has been recommended as a standard of care. Recent data suggests that endoscopic treatment might be curative also in such patients with 'high-risk' EEC.
**Aims & Methods:** To compare outcomes of endoscopic vs. surgical treatment in patients with 'high-risk' EEC. 'High-risk' cancer was defined as any cancer with sm invasion or mucosal cancer with at least one of the following: poor (G3/G4) differentiation, A+ and/or L+ (blood or lymphatic vessel invasion) and high tumor cell dissociation (TCD3). The main outcome measurement was defined as tumor-free survival after surgical/endoscopic treatment.
A single-center, prospective study. Patients with EEC underwent endoscopic resection (ER) or endoscopic submucosal dissection (ESD). Based on staging, patients with 'high-risk' EEC were referred for surgery if there were no contraindications. All other patients continued (if necessary) in endoscopic treatment which consisted of further sessions of ER and/or radiofrequency ablation (RFA). After treatment, all patients have been followed up by a median of 27 months (range 3–144).
**Results:** A total of 43 patients with 'high-risk' EEC were diagnosed: 15 patients (35%) had T1a cancer with 'high-risk' features (L+: 1; TCD3 with L+: 1; G3 with A+ and L+: 1; G3 with TCD3: 5; TCD3: 7) and 28 patients (65%) had cancer with submucosal invasion (sm1: 13; sm2: 6; sm3: 9); 37 patients had adenocarcinoma (AC) and 6 patients squamous carcinoma (SCC).
Fifteen patients (35%) were referred for esophagectomy and 28 patients (65%) continued in endoscopic treatment. In one patient, the planned esophagectomy was abandoned due to tumor generalization (AC) found during the operation, and he has since undergone chemotherapy.
Among 14 patients who underwent esophagectomy, local residua of malignancy after endoscopic treatment were present in 3 patients (21%) and lymph node (LN) metastases have not been detected in any of 210 investigated LN. During the follow-up, none of the patients has shown signs of generalization or a local tumor relapse. In patients with endoscopic treatment, a complete remission of neoplasia was achieved in 22/24 patients (93%) during a median of 2 (range 1–4) treatment sessions. Tumor-free survival has been 100% in patients treated by surgery and 92% (CI 81–100%) by endoscopic treatment (NS) vs. surgery. Cancer related mortality has been zero in both groups.
**Conclusion:** Endoscopic treatment provides a long-term remission or cure in a considerable number of patients with 'high-risk' early esophageal cancer, representing a valid alternative to surgery. The broadened indications for radical endoscopic treatment should be further defined.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0468 DEVELOPMENT AND VALIDATION OF A TRAINING MODULE ON THE USE OF ACETIC ACID CHROMOENDOSCOPY (AAC) TO DETECT BARRETT'S NEOPLASIA

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**Introduction:** AAC enhances the ability to correctly identify Barrett's neoplasia and is increasingly used by both expert and non-expert endoscopists. However, despite its increasing use, there is no validated training strategy to achieve competence.
**Aims & Methods:** The aim of our study was to develop a validated training tool in the technique of using AAC, lesion recognition and a novel acetic acid classification and evaluate its impact and effectiveness. A validated assessment of 40 images and 20 videos was developed. 13 endoscopists with experience of Barrett's endoscopy but no formal training in AAC (7 consultants, 6 nurse endoscopists) underwent training. Participants underwent: baseline assessment (1)®online training®assessment (2) ®interactive seminar®assessment (3).
**Results:** Endoscopists with vast experience in Barrett's endoscopy lack lesion recognition skills with AAC, consultants perform no better than nurse-endoscopists. There were statistically significant increases in accuracy, sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) following the online training module (Table 1). There was additional gain from the interactive live workshop. Improvement was also seen in inter-observer agreement.
**Conclusion:** 1. Our data demonstrate the need for training as baseline performance, even by experts, was poor 2. We were successful in developing and validating an online training and testing tool for acetic acid chromoendoscopy for Barrett's neoplasia 3. Low pre-training scores amongst users and non-users demonstrated the need for training tool 4. Training intervention with our tool improves the accuracy of endoscopists meeting the ASGE PIVI standards for sensitivity and NPV 5. The training tool increases the endoscopist's degree of confidence in the use of AAC 6. The training tool also leads to shift in attitudes of endoscopists from Seattle protocol towards AAC guided biopsy protocol for Barrett's surveillance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Abstract No: P0468**

**Table 1:** Performance of educational intervention at each stage of training tool, *p < 0.05 The training intervention with our tool led to a significant improvement in the endoscopist confidence in AAC, with the mean pre-training confidence level rising from 2.5 (5-point scale) to 3.9 post-training (p < 0.001). The training module led to a significant shift to the willingness of the endoscopists in changing practise from Seattle protocol to AAC-targeted biopsy with mean pre-training score of 2.6 (5-point scale) rising to 3.8 post-training(p < 0.001).

| | Accuracy | Sensitivity | Specificity | PPV | NPV | Kappa |
|---|---|---|---|---|---|---|
| **Images** | | | | | | |
| **Baseline** | 79% 0.75–0.83 | 83% 0.79–0.86 | 76% 0.73–0.79 | 76% 0.72–0.79 | 83% 0.79–0.86 | 0.48 |
| **Online training** | 86%* 0.83–0.88 | 95%* 0.92–0.97 | 79% 0.76–0.81 | 80% 0.78–0.82 | 94%* 0.91–0.98 | 0.67 |
| **Interactive Seminar** | 82%* 0.80–0.84 | **98%** 0.95–0.99 | 68% 0.66–0.69 | 74% 0.72–0.75 | **97%*** 0.94–0.99 | 0.75 |
| **Videos** | | | | | | |
| **Baseline** | 78% 0.72–0.83 | 73% 0.67–0.78 | 83% 0.77–0.88 | 81% 0.75–0.87 | 76% 0.70–0.80 | 0.41 |
| **Online training** | 82% 0.77–0.86 | 91%* 0.86–0.95 | 74% 0.69–0.78 | 78% 0.73–0.81 | 89%* 0.83–0.94 | 0.51 |
| **Interactive Seminar** | 79% 0.75–0.81 | **99%*** 0.95–1.0 | 60% 0.56–0.61 | 71% 0.68–0.72 | **98%*** 0.91–1.0 | 0.63 |

## P0469 A RANDOMIZED CONTROLLED STUDY COMPARING SEMI-COVERED STENTS VERSUS FULLY-COVERED STENTS OF A NOVEL DESIGN WITH REGARD TO STENT MIGRATION, IN PALLIATIVE TREATMENT OF OESOPHAGUS AND CARDIA CANCER

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**Introduction:** It is well-documented that stenting is the best palliative treatment for advanced oesophagus- and cardia-cancer when it comes to relief of dysphagia. However, which kind of stent that is most favorable has not been established. Earlier designs of fully-covered oesophageal stents had the acknowledged disadvantage of a higher risk of migration. In this study we compared a newer design of a fully-covered stent (Wallflex®) with a widely used semi-covered stent (Ultraflex®). Migration more than 20 mm was the primary outcome. Effects on dysphagia, QoL and need for re-intervention were also investigated.

**Aims & Methods:** Ninety-five patients with dysphagia secondary to a non-curable oesophagus/cardia cancer were randomized, in a prospective multi-center setting, to receive either the newer fully-covered stent (n = 48) or the conventional semi-covered stent (n = 47). The follow-up examinations were scheduled at one week, four weeks and three months, entailed a chest x-ray, dysphagia scores and QoL measurements.

**Results:** 13.9% of patients with fully covered stents experienced stent-migration compared to 25.6% with partially-covered stents at three months; a difference which was not significant. During total survival time the difference in migration were 20.1% vs 37.2% with a tendency towards significance (p = 0.068) in favor for the fully-covered group.

Dysphagia was measured with Watson and Ogilvie scores and with the dysphagia module in the quality of life measurements (QLQ OG-25). On average, there was a tendency to a better result for the fully-covered design with the two latter dysphagia instruments (p = 0.081 and p = 0.067), but only at three months. There was no significant difference in Quality of life (QLQ-C30) between groups at any time point. No difference in technical failures was detected, but a trend towards more re-interventions in the semi-covered group (p = 0.083) was seen.

**Conclusion:** This study suggests that the risk of migration is not increased when using a fully-covered stent compared to the conventional semi-covered stent. The potential benefit of the former is reflected by somewhat better effects on dysphagia relief in those with longer life expectancy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0470 LYMPHOVASCULAR INVASION MAY BE MORE RELEVANT TO NODAL METASTASES THAN SUBMUCOSAL MASSIVE INVASION IN EARLY-STAGE ESOPHAGEAL SQUAMOUS CELL CANCERS: A RETROSPECTIVE ANALYSIS IN 29 CASES

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**Introduction:** Endoscopic submucosal dissection (ESD) for early-stage esophageal squamous cell cancer (ESCC) s is gaining acceptance as one of curative treatment options. With regard to the possibility of nodal metastasis, lesions invading muscularis mucosae (MM) or deeper or positive lymphovascular invasion are thought to require additional treatments even though they are completely resected endoscopically. However, which of the two factors (tumor invasion or lymphovascular involvement) contribute more to the probability of nodal metastases has not been fully investigated. Therefore, we retrospectively assessed non-curative ESCC cases after ESD to compare the potential risk of nodal metastasis between these two histological findings.

**Aims & Methods:** We identified 163 patients who underwent initial ESD from June 2010 to September 2015. Of these, the invasion depth was MM or SM in 31 lesions in 30 patients. Out of 30 patients, we assessed the clinical courses of 29 patients who could be monitored after ESD.

**Results:** The mean age was 65.5 years old. Males and females were 24 and 5, respectively. The mean size of lesions was 30.1 mm. En bloc resection rate was 100% (29/29). Complete resection rate was 96.8% (28/29). Clinical courses after ESD were observation (17), surgery (8), chemoradiotherapy (2) or chemotherapy (1), respectively. The depths of invasion were MM/SM1 in 25 and SM2 in 4, respectively. Of the 25 patients (MM/SM1) and 4 patients (SM2), 5 patients and 3 patients underwent surgery, respectively. Although there was no pathological residual cancer after surgery, lymph node metastasis rate of MM/SM1 and SM2 was 40% (2/5) and 33% (1/3), respectively (p = 0.8214). Lymphovascular involvement was positive in 6 patients (20.7%). Of these, each 4 patients with or without ductal invasion underwent surgery. There was a tendency that lymph node metastasis rate was higher (3/4, 75%) in positive ductal invasion cases than in negative cases (0/4, 0%), without significant difference (p = 0.0714). The mean observational period was 25 months. The overall survival rate was 96.8% (28/29). There was no esophageal cancer death.

**Conclusion:** Lymphovascular involvement may contribute more to the probability of nodal metastasis than the depth of invasion. Additional treatments after ESD should be considered in cases having ductal invasion. On the other hand, the data implied that no further treatment could be avoided after ESD in some non-curative cases without ductal invasion. ESD for ESCCs as a staging measure may be acceptable especially in patients who are reluctant to undergo radical treatments due to comorbidities.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0471 CLINICAL SIGNIFICANCE OF GLASGOW PROGNOSTIC SCORE FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA AFTER ESOPHAGECTOMY

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**Introduction: Depth of tumor invasion and lymph node metastasis** are well-known prognostic factors in esophageal squamous cell cancer (ESCC). Inflammation-based Glasgow prognostic score (GPS), which is based on a combination of C-reactive protein (CRP) and albumin measurements, has been reported to have a prognostic value for several types of cancer, such as colorectal cancer and gastric cancer. However, the value of GPS for ESCC remains unclear.

**Aims & Methods:** The aim of this study was to investigate the prognostic value of GPS for ESCC after R0 esophagectomy. A total of 328 patients with ESCC who underwent R0 radical esophagectomy with 2- or 3- field lymphadenetomy between January 2000 and December 2014 were identified from a prospectively collected database. Prognostic factors were investigated according to the depth of tumor invasion. Patients with both an elevated CRP (≥10 mg/L) and low albumin (<35 g/L) levels were allocated a score of 2. Patients with only one of these abnormalities were allocated a score of 1, and those with normal CRP and albumin levels were allocated a score of 0.

**Results:** There were 290 males and 38 females, with a median age of 64 years (39–87 years). Of these, 112 (34%) had pT1 tumor, 53 (16%) had pT2 tumor, and 163 (50%) had pT3 tumor. The 5-year overall survival (OS) rate for the whole group was 60%, with a median follow-up of 82.2 months. The 5-year OS was 70% for pT1/2 ESCC and 50% for T3 (pT1/2 vs pT3, P = 0.0001). Two hundred thirty-seven patients had GPS 0 (72.5%), 67 had GPS 1 (20.5%), and 23 had GPS 2 (7%). 1) Prognostic factors for pT1/2 ESCC. In univariate analysis, age (<65 vs ≥65, P = 0.0008), GPS (0 vs 1/2, P = 0.0018), and other primary malignancy (no vs yes, P = 0.0388) were found to be factors affecting the survival. Other factors including gender (female vs male), tumor length (<6 cm vs ≥6 cm), tumor location (lower vs middle/upper), multifocal neoplasia (no vs yes), lymph node

metastasis (pN0 vs pN1–3), histologic grade (1 vs 2/3), lymphadnectomy (3F vs 2F), and postoperative morbidity (no vs yes) did not affect the survival. In multivariate analysis, GPS (HR: 2.814, 95%CI: 1.530–5.013, P = 0.0012) and age (HR: 2.488, 95%CI: 1.4643–4.2990, P = 0.0007) were found to be independent prognostic factors. 2) Prognostic factors for pT3 ESCC. In univariate analysis, gender (P = 0.0389), lymph node metastasis (P = 0.0054), and histologic grade (P = 0.0231) were significantly associated with OS. In multivariate analysis, only lymph node metastasis was an independent prognostic factor (HR: 1.789, 95%CI: 1.057–3.219, P = 0.0293).
**Conclusion:** Prognostic factors were different according to the depth of tumor invasion. GPS has prognostic value in patients with pT1-2 ESCC who underwent R0 esophagectomy. However, GPS does not have the prognostic significance in patients with pT3 ESCC. GPS might be more practical when used in combination with tumor-related factors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0472 MISSED OESOPHAGOGASTRIC CANCERS AT ENDOSCOPY, WHAT CAN WE LEARN FROM RETROSPECTIVE AUDIT?

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**Introduction:** Studies based on retrospective analysis in England found 6–14% of patients with oesophagogastric malignancy had an endoscopy within the 3 previous years. This study aims to establish the incidence of oesophagogastric (OG) missed cancers during endoscopy and identify possible risk factors based from our experience in a district general hospital in the UK which serves a population of half a million patients. Possible risk factors suggested from other studies include concurrent UGI Bleeding and use of sedation.
**Aims & Methods:** This is a retrospective study of all patients diagnosed with OG cancers from March 2014–15. We identified those patients who underwent an endoscopy within 3 years before the diagnosis. The indications, findings, endoscopist seniority and type of sedation were recorded. The information was extracted from computerised endoscopy and histology records. We also compared our findings with the previous years and 2013–14.
**Results:** 71 patient were diagnosed with upper GI cancer over one year period and 5 (7%) had a previous endoscopy done within the last 3 years. 3 cases were oesophageal and 2 cases were gastric cancers. Mean age at diagnosis was 76 years (range 62–89). The endoscopy was performed mainly by Consultant in 60% of cases. Two cases needed a third endoscopy in order to diagnose the cancer. In two cases, one with Barrett's and one failed intubation, the repeated planned endoscopy did not happen in a timely manner. In one case, oesophageal cancer was mistaken for food residue in two occasions. The fourth case was a patient with Barrett's who underwent surveillance and cancer was missed on biopsy and the last case was a patient with gastric ulcer which was not initially biopsied because of dual anti-platelets therapy.
**Conclusion:** We have identified a small number (7%) of upper GI cancer missed during endoscopy in the last year audit**.** The reported incidence seem to be similar to a previous audit conducted in our hospital (9%) and to a larger English study. The presence of sedation or the level of endoscopist seniority did not seem to be related to missed cancer. We stress the importance of performing quality endoscopy, of timely follow-up endoscopies and to improve the standard of OG endoscopy nationally, with quality indicators for gastroscopy and standardised teaching as recommended by the British Society of Gastroenterology.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0473 THE OUTCOME OF ESOPHAGO-GASTRIC JUNCTIONAL ADENOCARCINOMA TREATED BY ESD AND ANALYSIS FOR THE RISK FACTOR OF LYMPH NODE METASTASIS

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**Introduction:** Esophago-gastric junctional adenocarcinoma (EGJAC) has been increasing in Japan. The risk of lymph node metastasis (LNM) of gastric adenocarcinoma (GAC) and esophageal squamous cell carcinoma (ESCC) is different. That of GAC corresponds with invasion depth, histology, size, ulcer scar and vascular invasion. And, that of ESCC corresponds with only invasion depth and vascular invasion. And, that of EGJAC is still unclear.
**Aims & Methods:** The aim of this study is to investigate the outcome of superficial EGJAC treated by ESD and the risk factor of LNM in superficial EGJAC. Ninety four patients (80 males and 14 females) with EGJAC treated by ESD from Jan. 2000 to Dec. 2012 were enrolled to this retrospective study. EGJAC was defined as adenocarcinoma located between 1 cm oral and 2 cm anal from EGJ. The median age and follow up period were 74 and 73 months, respectively. The median diameter of the lesions was 18 mm. Protuberant, flat and depressed type was 44, 3 and 47 lesions, respectively. T1b was sub-classified into T1bSM1 (500 micrometer or less) and 2 (501 micrometer or bigger). T1aM, T1bSM1 and T1bSM2 were 67, 15 and 12, respectively. Dominant histology, differentiated and poorly differentiated adenocarcinoma were 90 and 4 lesions, respectively.
**Results:** 1. Complete resection rate was 100%. R0 rate resection was 99% (93/94). 2. Complications: The bleeding during ESD and delayed bleeding required blood transfusion was 0% and 1% (1/94). The perforation during ESD and delayed perforation was 1% (1/94) and 0%. Stenosis was 11% (10/94), and all of 10 cases were treated by endoscopic balloon dilatation. 3. Local recurrence rate was 0%. 4. The risk factors of LNM (Univariate analysis) a. Invasion depth; The rate of LNM was 0% (0/82) in T1aM to T1bSM1 and 8% (1/12) in T1bSM2 (p = 0.12277). b. Histological type; The rate of LNM was 0% (0/90) in well differentiated adenocarcinoma (WDA) and 25% (1/4) in poorly differentiated adenocarcinoma (PDA) (p = 0.00426). c. Histology of T1b; The rate of LNM of WDA and PDA were 0% (0/22) and 20% (1/5) in poorly differentiated adenocarcinoma (p = 0.11852). d. Lymphatic invasion; The rate of LNM was 33% (1/3) in positive and 0% (0/91) in negative (p = 0.0319). e. Tumor size, ulcer scar didn't correlate with LNM; 5. The risk factors of LNM (Multivariate analysis) Lymphatic invasion (p = 0.03) and PDA (p = 0.05) were the risk factors of LNM.
**Conclusion:** The outcome of superficial EGJAC treated by ESD was excellent. Lymphatic invasion and PDA were the risk factors of LNM of EGJAC. The guide lines of GAC rather than ESCC should be indicated for EGJAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0474 CHARACTERISTICS AND RISK FACTORS FOR SOLITARY NON-AMPULLARY DUODENAL CARCINOMA

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**Introduction:** Non-ampullary duodenal carcinoma (NADC) is rare, and its characteristics and risk factors are not well-known.
**Aims & Methods:** The aim of this study was to clarify clinical characteristics and risk factors for solitary NADC. From the cancer registry database from 2003 to 2015 in a prefectural cancer center, patients diagnosed as non-ampullary duodenal carcinoma were extracted. Patients with duodenal tumors such as neuroendocrine tumors, lymphoma, stromal tumor, metastatic tumor, ampullary tumors and familial adenomatous polyposis were excluded. For each NADC patient, 2 age/sex-matched controls were selected from medical checkup recipients in the same hospital. Smoking and drinking habits, history of colorectal adenoma/carcinoma, infection status of *Helicobacter pylori* (*H. pylori*), grade of gastric atrophy, diabetes, other malignancy and familial history were compared between the groups.
**Results:** A total of 160 NADC in 156 patients (male/female: 103/53) and 312 controls were assessed. The median age of NADC patients was 64 (range 31–90) and median body mass index was 22 (range 15–31). Most of NADC were located in the second portion (121/160, 76%), histology was mostly differentiated adenocarcinoma (144/160, 90%), the clinical/pathological depth was T1 in 99 (63%), T2 or more in 57 (37%) patients. In total, number of smoking habit (past or current), *H. pylori* infection, and moderate to severe atrophic gastritis were significantly higher in NADC patients. There was no difference among history of colorectal adenoma/carcinoma and familial history between the groups. In male NADC patients, number of past history of other malignancy was also significantly higher. In female NADC patients however, number of smoking and drinking habits were the only significant factors.
**Conclusion:** The frequency of NADC was higher in men. The common risk factor for NADC of both genders was smoking.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0475 EFFECT OF VONOPRAZAN IN ARTIFICIAL ULCER HEALING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Anti-secretory agents, proton pump inhibitors (PPIs) and histamine H2 receptor antagonists (H2RAs), have already been the standard management for artificial gastric ulcers after endoscopic surgeries. Vonoprazan is a new type of anti-secretory drug, Potassium-Competitive Acid Blocker (P-cab). This drug could involve stronger and more rapid anti-secretory effect than common used PPIs. Vonoprazan so far indicated the equal or superior efficacy for peptic gastric or duodenal ulcer compared to the existing PPI, Lansoprazole. However, the effect of Vonoprazan for ESD-related procedure and adverse events is unclear.
**Aims & Methods:** We preliminary conducted this study to clarify the effect of Vonoprazan to the ESD-related gastric ulcer healing compared to Lansoprazole. We prospectively analyzed consecutive patients treated between April 2015 and March 2016 at Hiraka General Hospital. Patients were randomly allocated to two groups just after the ESD procedure by the following pharmacotherapy for 4 weeks: Group V (treated by Vonoprazan 20 mg) and Group L (treated by

Lansoprazole 30 mg). The primary outcome was the epithelial regeneration rate of the artificial ulcer base 2 weeks after ESD. The secondary outcomes were the diminution rate of the artificial ulcer 2 or 4 weeks after ESD and the occurrence rate of adverse events.
**Results:** A total of 60 patients were enrolled (30 cases in Group V and 30 cases in Group L). In Group V, the epithelial regeneration rate was significantly accelerated (P = 0.0007), and the diminution rate 2 or 4 weeks after ESD was significantly higher (P = 0.0060 / 0.0069) compared to Group L. There were no adverse events in both Groups.
**Conclusion:** P-CAB indicated to posses a rapid artificial ulcer healing compared to the common used PPI in this study. This suggested that P-CAB could be potential pharmaco-therapeutic choice after gastric ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0476 THE CORRELATION BETWEEN HISTOLOGICAL GASTRITIS STAGING- "OLGA/OLGIM" AND SEROLOGICAL PEPSINOGEN TEST IN RISK ASSESSMENT OF GASTRIC CANCER IN CHINA

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**Introduction:** The combination of serum pepsinogen (PG) level and serum anti-*Helicobacter pylori* IgG antibody, "ABC method", has been suggested to serve as a useful predictive marker for patients with gastric cancers. The available classifications of gastritis, known as the Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastritis Intestinal Metaplasia (OLGIM), have been gradually accepted and used in screening for gastric cancer in recent years.
**Aims & Methods: Aim**: To assess whether OLGA staging system and OLGIM staging system are consistently stratified patients according to the ABC method and applicable in the screening for gastric cancer. **Methods**: The OLGA or OLGIM staging system ranks the GC risk according to both the topography and the severity of gastric atrophy or intestinal metaplasia. A total of 331 enrolled consecutive patients (140 men and 191 women) who underwent endoscopy with consecutive biopsy sampling (A set of at least 5 biopsy samples) were retrieved and reassessed according to both the OLGA and the OLGIM staging systems. Serum pepsinogen tests, including the levels of PG I, PG II, PGI/PFII (PGR) and *H. pylori* antibody, were also measured to assess the presence of atrophic gastritis. Results were presented as gastritis stage serum pepsinogen level and *H. pylori* status.
**Results**:All patients were assessed applying the OLGA and OLGIM criteria with a mean age of (54.7 ± 10.8) years. Overall, 116 (27.9%) and 154 (37.1%) patients were classified as stage I-IV according to OLGA and OLGIM. Patients among OLGA or OLGIM stage III-IV were presented with a lower level of serum PGI and PGR (P < 0.05), especially for stage-IV (P = 0.01). Meanwhile, according to the result of serum pepsinogen tests, 214 (64.7%) patients were classified into group A, 106 (32.0%) patients into group B, 4 (1.2%) patients into group C and 7 (2.1%) patients into group D, respectively. There exists connections between OLGA, OLGIM stratifications and ABC method in patient stratification for gastric mucosal atrophy assessment (P = 0.002, P = 0.004).
**Conclusion:** Gastritis staging, including OLGA and OLGIM, combined with serum pepsinogen levels, provide prognostically important information on the cancer risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0477 UPCOMING PARADIGM SHIFT OF GASTRIC CANCER RISK: INCREASE OF H. PYLORI NEGATIVE GASTRIC CANCER AND THEIR RISK FACTORS

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**Introduction:** Although the prevalence of *H. pylori* infection has gradually decreased recent two decades, the incidence of gastric cancer has not decreased. The incidence of *H. pylori* negative gastric cancer (HPNGC) has been reported as below 10% before 2010. The tumor characteristics of HPNGC have been evaluated but host habitual factors have not been known. We evaluated the incidence and host habitual factors of HPNGC in South Korea.
**Aims & Methods:** A total of 394 gastric cancer patients underwent rapid urease test and serum *H. pylori* IgG test and completed the questionnaires for personal history and diet habits from March 2014 to Oct 2015 in a single medical center. *H. pylori* positive gastric cancer (HPPGC) was defined as current *H. pylori* infection and HPNGC was defined as negative current infection and negative serum HP IgG and no history of *H. pylori* eradication. Past infection was defined as current *H. pylori* negative with presence of *H. pylori* eradication or positive serum *H. pylori* IgG.
**Results:** The portion of HPNGC, HPPGC, and past infection was 34% (n = 134), 50% (n = 198), and 16% (n = 62), respectively. HPNGC was related with old age comparing to HPPGC (64.7yr vs 61.9yr, P = 0.025) and early menopause (48.0yr vs 50.8yr, p = 0.014). Low fruit diet was higher in HPNGC than HPPGC (59.4% vs 47.9%, p = 0.041) and low soy-tofu diet was also higher in HPNGC than HPPGC (31.6% vs 19.7%, p = 0.014). In multivariate analysis, age increased the risk of HPNGC (odd ratio [OR] 1.03, 95% confidence interval [CI] 1.01–1.05), whereas high fruit diet (OR 0.58, 95% CI 0.36–0.94) and high soy-tofu diet (OR 0.60, 95% CI 0.30–0.99) decreased the risk of HPNGC.
**Conclusion:** The incidence of HPNGC was high comparing to previous reports and they are related to increasing age, low fruit diet, and low soy-tofu diet comparing to HPPGC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0478 NEGATIVE PATHOLOGIC RESULTS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Endoscopic submucosal dissection (ESD) is largely used for gastric superficial neoplasm (gastric adenoma or EGC), although in some cases the negative results of the pathological group after ESD leads to confusion.
**Aims & Methods:** After ESD forgastric adenoma or EGC by endoscopic forceps biopsy, we evaluated the causes and factors with negative pathologicresult after ESD. Between December 2008 and July 2015, a total of 1379 patients were performed after endoscopic forceps biopsy. Weanalyzed the causes and factors that are associated with negative pathology.
**Results:** The incidence of patients with a negative pathology after ESD was 2.0% (28/1379). Factors related to negativepathologic findings were small tumor size and surface area. The reasons of negative pathologic lesions after ESDwere as follows: complete removal during endoscopic forcep biopsy, overestimation of EFB pathology and incorrectlocalization of ESD site.
**Conclusion:** Small tumor size and surface area were associated with negative pathologic result after ESD. When negativepathologic results were reported after ESD, a review of the previous endoscopic biopsy tissue pathology andcontinued observation of the lesion is needed, because of the possibility of an incorrect localization during ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0479 EFFICACY AND SAFETY OF A PATIENT-POSITIONING DEVICE (EZ-FIX) FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF GASTRIC EPITHELIAL NEOPLASM

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**Introduction:** Endoscopic submucosal dissection (ESD) has been widely accepted as an excellent treatment for gastric epithelial neoplasm. Although ESD has its advantages, the technique of ESD is complicated and requires considerable expertise and a prolonged operation time and at least moderate to deep level of sedation. So, we think that fixing the position of patient can minimize patient movement and can achieve safe and successful ESD procedure outcomes. EZ-FIX is a patient-positioning device that uses polyethylene particles and compressed air that is expected to contribute to procedure efficacy and safety by fixing the position of the patient.

**Aims & Methods:** To assess the efficacy of a patient positioning device (EZ-FIX) during endoscopic submucosal dissection (ESD) for gastric epithelial neoplasm. In this prospective study, a total of 86 patients who had been diagnoesd with gastric adnoma or early gastric cancer were randomized to the EZ-FIX (n = 44) and non-EZ-FIX (n = 42) group. During ESD, midazolam and propofol was titrated to provide an adequate level of sedation, and patient's movement score was measured. The endoscopist completed a questionnaire after ESD, using a 10-cm visual analog scale (VAS), which assessed the level of satisfaction with sedation and overall satisfaction with the procedure. In the EZ-FIX group, a contribution of EZ-FIX to stable ESD was assessed and diviedeinto four categories of none, low, medium and high. We defined the contribition group from low to high categories. Patients also completed a questionnaire, using a 10 cm VAS, which assessedpost-ESD myalgia, overall satisfaction with procedure and an uneasiness to EZ-FIX use.
**Results:** There was no significant difference between the EZ-FIX and non-EZ-FIX groups in terms of age, gender, BMI, ASA score, lesions' endoscopic and histological findings and dose of sedatives. EZ-FIX group just took a longer procedural time than the non-EZ-FIX group (28.1 ± 24.2 minvs19.6 ± 12.0 min, p = 0.044). Clinical outcomes including an en bloc and complete resection rate, procedure related complications, endoscopistsatisfaction with sedation and overall satisfaction with procedure did not differ between the two groups. In the EZ-FIX group, 16 patients (36.4%) were a contribution group. Subgroup analysis between the contribution and non-contricution groups revealed that the contribution group had a larger lesion size (24 ± 19 mm vs 15 ± 10 mm, p = 0.043) with a longer procedural time (38.0 ± 33.9 mind vs 22.4 ± 14.2, p = 0.037), and had a higher patient's movement score (p = 0.000) with a higher dose of propofol (p = 0.004) and pethidine (p = 0.001). Endoscopist satisfaction with sedation (7.5 ± 1.0 vs 9.5 ± 0.5, p = 0.00) and overall satisfaction with the procedure (8.4 ± 1.0 vs 9.2 ± 0.8, p = 0.01) was lower in the contribution group than the non-contribution group. The results of the patients'questionaire survey did not differ significantly between the two groups.

Clinical outcomes of the ESD procedure in the EZ-FIX and non-EZ-FIX group

| | EZ-FIX (n = 44) | Non-EZ-FIX (n = 42) | P value |
|---|---|---|---|
| En bloc resection rate | 100 | 97.6 | 0.303 |
| Complete resection rate | 97.7 | 97.6 | 0.973 |
| Procedure related complications (%) | | | |
| Bleeding | 1 (2.3) | 0 (0) | 0.326 |
| Perforation | 0 (0) | 0 (0) | |
| Unstable vital sign | | | |
| Below 90% in SaO2 for ≥30 s | 0 (0) | 0 (0) | |
| ↓20 mm = Hg in BP | 0 (0) | 0 (0) | |
| ↓20% in PR | 0 (0) | 0 (0) | |
| Endoscopist satisfaction with sedation | 8.8 ± 1.2 | 8.4 ± 1.6 | 0.240 |
| Endoscopist overall satisfaction with procedure | 8.9 ± 0.9 | 8.8 ± 1.4 | 0.632 |

**Conclusion:** To achieve successful outcomes, patient's cooperation is very important during ESD. In this study, we think EZ-FIX is an effective tool for patients with incomplete sedationand who are expected to take a long procedure time with a large lesion size, especially more than 2 cm.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0480 USEFULNESS OF A NOVEL MAGNIFYING LCI WITH INDIGO CARMINE DYE IN THE DIFFERENTIAL DIAGNOSIS OF GASTRIC SMALL DEPRESSIVE LESIONS


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**Introduction:** Magnifying endoscopy using image-enhanced endoscopy (M-NBI or M-BLI) has been reported to be useful for the accurate diagnosis in the GI tract compared with white-light imaging (WLI) endoscopy [1, 2]. However, NBI or BLI produces monochromatic images only, thus conventional magnifying endoscopy findings are difficult to interpret in some situations. Recently, Linked Color Imaging (LCI) was developed using a laser endoscopic system, which emphasizes the contrast of reddish color. We discovered LCI with indigo carmine dye (Chromo-LCI), which can add information of color image to magnifying endoscopy. Thus, Chromo-LCI is considered a novel image-enhanced endoscopy, contributing to improve visualization of the microstructures and microvessels of the superficial gastric mucosa.
**Aims & Methods:** The aim of this retrospective, cross-sectional image evaluation study was to investigate the usefulness of M-Chromo-LCI for the differential diagnosis of gastric lesions. We collected 100 consecutive gastric small depressive lesions between December 2014 and March 2016. The inclusion criteria were as follows: lesions estimated 10 mm; lesions diagnosed as noncancerous or cancer on biopsy or endoscopic resection specimens; and endoscopic images of the same lesions taken under the same conditions using M-BLI and M-Chromo-LCI. The expert selected one endoscopic image for each modality that could adequately depict whether a lesion is cancer or noncancerous. The endoscopic images were randomly displayed for each modality, and independently reviewed by six endoscopists (3 experts and 3 non-experts) without prior knowledge of the histologic findings of the lesions. The diagnostic accuracy and interobserver agreement for WLI, M-BLI, and M-Chromo-LCI were then compared.
**Results:** For the experts, M-BLI showed a statistically significantly higher diagnostic accuracy, sensitivity, and specificity compared with WLI (82.7% vs 67.0%, $P < 0.05$, 80.6% vs 66.1%, $P < 0.05$, and 85.2% vs 68.1%, $P < 0.05$, respectively). M-Chromo-LCI showed a statistically significantly higher diagnostic specificity compared with M-BLI (95.6% vs 85.2%, $P < 0.05$), but the diagnostic accuracy of M-BLI (82.7%) and M-Chromo-LCI (87.7%) did not differ significantly. For the non-experts, M-BLI showed a statistically significantly higher diagnostic accuracy and sensitivity compared with C-WLI (69.3% vs 52.3%, $P < 0.05$, 77.6% vs 52.1%, $P < 0.05$, respectively). M-Chromo-LCI showed a statistically significantly higher diagnostic accuracy and specificity compared with M-BLI (79.7% vs 69.3%, $P < 0.05$, 74.1% vs 59.3%, $P < 0.05$, respectively). For the experts, interobserver agreement indicated fair agreement for C-WLI, moderate agreement for M-BLI, substantial agreement for M-Chromo-LCI (kappa values = 0.33, 0.52 and 0.77, respectively). For the non-experts, interobserver agreement indicated fair agreement for C-WLI and M-BLI, moderate agreement for M-Chromo-LCI (kappa values = 0.32, 0.33 and 0.43, respectively).
**Conclusion:** M-chromo-LCI enabled the accurate diagnosis of gastric small depressive lesions with good reproducibility, regardless of the reviewer's proficiency. Magnifying Chromo-LCI is expected to be powerful modality for the differential diagnosis of gastric lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0481 NEUTROPHIL LYMPHOCYTE RATIO VERSUS PLATELET LYMPHOCYTE RATIO IN PREDICTION OF SURVIVAL IN PATIENTS WITH GASTRIC ADENOCARCINOMA


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**Introduction:** The serum neutrophil lymphocyte ratio and platelet lymphocyte ratio are considered an easily assessable prognostic factor in cancer patients. We evaluated significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in predicting survival in patients with gastric cancer who had undergone gastric resection.
**Aims & Methods:** From 2003 to 2014, 192 patients who had undergone gastrectomy with curative intent for gastric adenocarcinoma were included. Data were retrieved from a prospective collected database. Neutrophil lymphocyte ratio and platelet lymphocyte ratio were calculated from lymphocyte and neutrophil counts on routine blood tests taken before surgery. Survival analyses were generated according to the Kaplan–Meier method. Univariate and multivariate analyses were carried out by the Cox proportional hazard model.
**Results:** Mean age of patients was 59 ± 12 (26–88). There were 68 female and 124 male patients. The median follow-up time for surviving patients was 24 months (range 1 to 32 months). None of the patients received a neoadjuvant treatment modality. Median preoperative neutrophil lymphocyte ratio was 3.7 ± 3.8 (range 0.34 to 33). A cut off value for neutrophil lymphocyte ratio was identified as of

2.3 according to ROC analysis. Multivariate analysis failed to show a statistically significant relationship between the neutrophil lymphocyte ratio and the overall survival with a p value of 0.167. When platelet lymphocyte ratio was analyzed it was seen that 155 was cut off according to ROC. Median preoperative platelet lymphocyte ratio was 1.9 ± 1.12 (range 11.6 to 614). Furthermore, Kaplan Meiere analysis depicted better overall survival in patients with platelet lymphocyte ratio less than 155.
**Conclusion:** Inflammatory mediators such as lymphocytes and platelets might promote progression of tumor cells. The results suggest that the elevated preoperative neutrophil lymphocyte ratio does not predict poor overall survival following resection for gastric adenocarcinoma. But elevated platelet lymphocyte ratio migth be used a marker to predict survival for these patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0482 THE INCIDENCE OF SYNCHRONOUS AND METACHRONOUS CANCERS AFTER ESD FOR UNDIFFERENTIATED-TYPE EARLY GASTRIC CANCER COMPARED TO AFTER ESD FOR DIFFERENTIATED- TYPE


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**Introduction:** Endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) in histology of undifferentiated-type (UD-type) adenocarcinoma is gradually prevailing from its minimally-invasive approach, though it is performed as clinical research in expanded indication of ESD according to Japanese Gastric Cancer Association (JGCA). There are still no report of multiple gastric cancers (synchronous or metachronous) comparing. The aim is to clarify the incidence of synchronous and metachronous gastric cancers after ESD for UD-type ECG.
**Aims & Methods:** We treated UD-type EGC in 237 patients by ESD which was preoperatively diagnosed as expanded indication (within 20 mm, intramucosal, without ulceration, UD-type adenocarcinoma) from May 2004 to October 2014, in Cancer Institute Hospital, Tokyo, Japan. Excluding the patients with past history of operation in stomach, 173 patients with UD-type ECG (UD group) was compared to the 173 patients with differentiated-type group (D group) treated by ESD. D group was randomly picked up matching their age and sex. Median observation period was 48.8 months. HP- was only diagnosed when the patients was HP- in 2 tests out of serum IgG, stool antigen and urease breath test and the patients didn't have gastric atrophy in endoscopy.
**Results:** We first compared the characteristics of patients and lesions between UD and D group. The ratio of male was 53%, 82% in UD and D group ($p < 0.01$). Tumor location in upper third was more frequent in UD than D group ($p < 0.01$). Tumor size was significantly smaller in UD group than in D group (10 mm vs 13 mm; $p < 0.01$). HP infection was less frequent in UD group than in D group (61% vs 100%; $p < 0.01$). The incident rate of synchronous cancer in UD and D group were 2.3% and 13.3% ($p < 0.01$). The cumulative incidence rate of metachronous cancer in UD group and D group were 0.7% and 10.5% in 3 years, 0.7% and 16.1% in 5 years, and 5.9% and 21.9% in 7 years. The incidence of metachronous cancer in UD group was significantly less frequent than D group by log-rank test ($p < 0.01$). Histology of multiple cancers were 3 D-type and 4 UD-type cancers in UD group, and 43 D-type cancers in D group ($p < 0.01$). Noteworthy, Hp- patients in UD group had only UD-type EGC, while patients in D group had only D-type EGC for synchronous and metachronous cancers.
**Conclusion:** Synchronous and metachronous cancers were less frequent in UD group than in D group. Histology of multiple cancers were different each other between D and UD group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0483 EARLY GASTRIC CANCER WITH MIXED HISTOLOGICAL COMPONENTS IS HIGH-RISK FOR LYMPH NODE METASTASIS


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**Introduction:** Endoscopic submucosal dissection (ESD) is minimally invasive therapy for early gastric cancer (EGC) and its application prevails gradually. After ESD is performed, we evaluate the obtained specimen histologically, and additional surgery becomes necessary when the lesion has the risk of lymph node metastasis. Several factors have been established as risks for lymph node metastasis. However, management of "mixed-type" lesions, which is consisted with differentiated and undifferentiated carcinoma, is still unclear.
**Aims & Methods:** The objective of the study is to clarify the clinicopathological significance of histologically mixed-type EGC. We retrospectively reviewed 593 consecutive EGC lesions in 528 subjects treated in our hospital (age (mean±SD) 69.9 ± 9.7), male/female 410/183). 362 were underwent ESD and 231 were underwent gastrectomy. We classified the obtained specimens into following four groups; purely undifferentiated type (PD, n = 471), mixed-type with predominantly differentiated part (MD, n = 34), purely undifferentiated type (PU, n = 55), and mixed-type with predominantly undifferentiated part (MU, n = 33). We examined the correlation between these types and following findings; location of the tumor, macroscopic type, tumor size, presence of lymphatic and vascular duct invasion, invasion depth of the cancer, and the existence of lymph node metastasis. Among subjects underwent gastrectomy, potential risk factor for lymph node metastasis including macroscopic type, tumor size, submucosal invasion depth, and the histological type (pure/mixed) were evaluated by multivariate logistic regression analysis.
**Results:** Subjects with PU type cancer were younger and held more female subjects than those with MU type ($p < 0.001$, $p < 0.05$). In macroscopic type, MD and PU type included more depressed lesions than PD and MU type, respectively ($p < 0.0001$, $p < 0.05$). Mean diameter of lesions of MD type were larger than that of PD type ($p < 0.0001$). MD and MU type were significantly associated with submucosal invasion than PD and PU type, respectively ($p < 0.0001$, $p < 0.001$) and this association was observed even among the lesion less than 20 mm, respectively ($p < 0.001$, $p < 0.05$). Multivariate analysis revealed that mixed-type (odds ratio (OR) = 3.1, 95% confidence interval (95%CI):1.2–8.3, $p = 0.02$) and the invasion depth (OR = 5.2, 95%CI: 1.6–2.3, $p = 0.01$) were significant risk factor for lymph node metastasis.
**Conclusion:** Regardless of tumor size, the factor of histologically mixed-type in EGC is an independent risk factor for lymph node metastasis. At evaluating the resected EGC, histological confirmation of whether the lesion is pure or mixed type should be considered.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0485 ANALYSIS OF PREDICTIVE FACTORS FOR VARIATION OF NEUTROPHIL COUNT DURING GASTROINTESTINAL CANCER CHEMOTHERAPY USING REAL WORLD DATA


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**Introduction:** Variation of neutrophil count is one of the most important indicator when monitoring the efficacy and safety of chemotherapy. Physicians are always required to balance between maintaining effective drug concentrations and avoiding febrile neutropenia. We know empirically that the variation of monocyte count can predict the variation of neutrophil count; only a small number of studies with relatively small sample size reported the association between the decrease of monocyte and neutropenia during chemotherapy. We hence searched for clinical data which could serve as indicative precursor factors of changes in neutrophil count through a time series analysis of laboratory data.
**Aims & Methods:** We retrieved 22 items of laboratory data, (red blood cell count, hemoglobin estimation, platelet count, neutrophil count, lymphocyte count, monocyte count, eosinophil count, blood urea nitrogen, creatinine, albumin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, γ-glutamyltransferase, lactate dehydrogenase, total bilirubin, sodium, potassium, chloride, calcium, serum glucose, C-reactive protein) at 54338 time points from 1807 gastrointestinal cancer patients who received chemotherapy using our clinical database system (CyberOncology®), that is integrated in electronic medical record of Kyoto University Hospital. The patients characteristics were as follows: The median age was 65 years (Range 31−87 years), and 1166 patients (65%) were men. The most common cancer type was colorectal (n = 592, 33%), followed by pancreas (n = 454, 25%) and stomach (n = 283, 21%). We applied Vector Autoregressive (VAR) models and estimated chronological models. Furthermore, we analyzed cause-effect relationship between neutrophil count and other laboratory data by impulse response assay in based on estimated VAR model.
**Results:** VAR model showed that monocyte count is one of the most relevant factor for predicting variation of neutrophil count. In addition to red blood cell

count and serum albumin were also found to be significant relationship with variation of neutrophil count ($P < 0.001$, Z-test).
**Conclusion:** We demonstrated that monocyte count is promising indicator for predicting variation of neutrophil count analyzing Real World Data obtained in daily clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0486 POTENTIAL ROLE OF MICRORNA-375 IN THE DIAGNOSIS OF CANCERS: A META-ANALYSIS


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**Introduction:** Several studies have investigated the association between abnormal circulating microRNA-375 (miR-375) expression and cancers and identified miR-375 as diagnosis biomarker for cancer. However, the results are inconsistent. Therefore, this meta-analysis aimed to assess the potential diagnostic value of miR-375 for cancer.
**Aims & Methods:** We searched PubMed, Embase, and Web of Science for publications concerning the diagnostic value of miR-375 for cancer. The bivariate meta-analysis model was employed to summarize sensitivity, specificity, and diagnostic odds ratio (DOR) for miR-375 in the diagnosis of cancer. Summary receiver operating characteristic (SROC) curve analysis and the area under the curve (AUC) were also used to check the overall test performance.
**Results:** A total of 588 cancer patients and 393 cancer-free individuals from 11 studies were contained in this meta-analysis. The summary estimates revealed that the pooled sensitivity is 78% (95% confidence interval (CI): 62%-88%), the specificity is 75% (95% CI: 61%-85%), the DOR is 10.40 (95% CI: 5.93–18.24), and the AUC is 0.83 (95%CI: 0.79–0.86).
**Conclusion:** Our data suggest that miR-375 profiling has a potential to be used as a screening test for various cancers, and more studies on the diagnostic value of miR-375 for cancer are needed in the future.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0487 CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN PATIENTS WITH EARLY GASTRIC CANCER UNDER 40 YEARS OLD


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**Introduction:** The clinicopathologic features of gastric cancer in young patients are different from those of older patients.
**Aims & Methods:** The aim of this study was to identify the clinicopathologic features of early gastric cancer (EGC) and clinical outcomes of endoscopic submucosal dissection (ESD) in young patients (≤40). From January 2006 and June 2014, 55 patients aged 40 years old or younger with newly diagnosed EGC underwent ESD at two tertiary hospitals. Clinicopathologic features of EGC and clinical outcomes ESD in these young patients were reviewed retrospectively, compared with those of standard ESD cohort in our hospital.
**Results:** 55 patients with 57 EGC lesions underwent ESD in young patients group. Compared with older patients in our standard ESD cohort (older than 40 years old, 806 patients with 831 EGC), female patient, superficial flat or depressed lesions, undifferentiated histology, deep mucosal invasion were more common in young patients group. En-bloc resection rate and complete resection rate were not significantly different between two groups (93.0% vs. 88.1%, $p = 0.264$; 71.9% vs. 67.1%, $p = 0.456$). Although high proportion of undifferentiated cancers in young patients group, curative resection rate was not lower for the young patients groups compared with older patients groups (73.7% vs. 69.6%, $p = 0.706$). Among 16 patients with non-curative resection, 4 patients underwent additional surgery and 1 patient underwent Argon Plasma coagulation at ESD ulcer margin. 9 patients were under close surveillance examination without additional treatment and there was no recurrent tumor. Median follow-up periods was $37.20 \pm 23.6$ months in young patients group. During follow-up periods, one patient was diagnosed synchronous cancer and underwent surgery.
**Conclusion:** Different clinicopathologic features of gastric cancer in young patients did not affect short-term outcomes of ESD compared with the older patients. ESD is a feasible treatment for young patients with EGC fulfilled expanded indication of ESD. However, long-term follow-up study is needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0488 FEASIBILITY OF COLD SNARE POLYPECTOMY FOR MULTIPLE DUODENAL ADENOMAS IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS: A PILOT STUDY


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**Introduction:** Duodenal, rather than colorectal, cancer is now the main cause of death in patients with familial adenomatous polyposis (FAP) after preventive proctocolectomy[1]. Endoscopic treatment for duodenal lesions is less invasive, but carries a high risk of complications such as bleeding or perforation[2, 3]. Therefore, watchful waiting has been recommended for patients with early-stage FAP[4]. Recently, cold snare polypectomy (CSP) for small colorectal polyps was reported to be safer than conventional hot snare polypectomy and equally effective[5, 6]. Therefore, we hypothesized that CSP was also safe for small duodenal adenomas in patients with FAP.
**Aims & Methods:** The aim of this study was to assess the feasibility of CSP for multiple duodenal adenomas in patients with FAP. This was a retrospective feasibility study including four consecutive FAP patients with multiple small duodenal adenomas who underwent CSP between July and October 2015. The primary outcome was complications during the 28 days post-CSP, such as bleeding or perforation. The secondary outcome was efficacy, using the staging system developed by Spigelman et al. to assess the severity of the duodenal polyposis, and to predict the risk of developing duodenal cancer[1]. We assessed Spigelman staging before CSP, and 2–4 months after CSP.
**Results:** The median patient age (two men, two women) was 45 years (range, 22–52 years), and all four patients had multiple duodenal adenomas (2–16 mm in size) located between the superior duodenal angle and the transverse duodenum. Two patients had Spigelman stage IV disease. The remaining two patients had Spigelman stage III disease. CSP was performed for a total of 126 duodenal polyps (2–16 mm in size) in the four patients (median 30 lesions/patient). Each patient underwent CSP once during the study period. During CSP, intra-procedural oozing occurred with most polyp excisions, but stopped spontaneously without endoscopic hemostasis in all cases. No prophylactic procedure, such as suturing with hemoclips or tissue shielding with polyglycolic acid sheets and fibrin glue, was performed for any of the cases. Although a total of 126 duodenal polyps were resected in these four patients, no cases experienced severe complications requiring emergency intervention (0%; 95% confidence interval: 0.00–0.02). Follow-up endoscopy was performed in all four patients a median of 2.75 months after CSP. Spigelman stage was downstaged in all cases at follow-up endoscopy.
**Conclusion:** CSP was feasible for multiple duodenal adenomas in patients with FAP. Although this was a pilot feasibility study, our results may support changing the current management strategy of duodenal adenomas in patients with FAP from a surveillance approach to a therapeutic approach.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0489 ORAL HEALTH-RELATED BEHAVIOR AMONG CANCER SURVIVORS IN KOREA USING POPULATION-BASED NATIONWIDE SURVEY

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**Introduction:** Cancer survivors may remain at life-long risk of developing oral complications. Despite worldwide recognition of the dangers of cancer, the oral health behavior among cancer survivors has not been fully addressed. To date, there are no data on oral health behavior among cancer survivors. In addition, few studies have investigated oral self-care and use of dental services by cancer survivors in Korea. Thus, we investigated oral health behavior among cancer survivors and compared to subjects without cancer history using nationwide survey.

**Aims & Methods:** We investigated oral health behavior among cancer survivors and compared to subjects without cancer history using nationwide survey. Data source: This study used the data from the Korea National Health and Nutrition Examination Survey conducted the Korea Centers for Disease Control and Prevention. Cancer survivors and controls Cancer survivors were defined as those who answered ''yes'' to the question, ''Have you ever been told by a doctor that you had cancer?''. Cancer survivors were asked about the site of their cancer and the age at diagnosis. The time since diagnosis was calculated as the difference between the age at the time of the survey and the age at diagnosis. Controls were defined as subjects who reported no cancer history. Oral health behavior: This study checked the tooth brushing frequency per day, the number of secondary oral products and oral health screening use. Secondary oral products included dental floss, mouthwash, interdental brush, and electric toothbrush. Statistical analysis: Oral health behavior of cancer survivors and controls were compared by chi-square tests and multiple logistic regression analysis. P values $< 0.05$ were considered statistically significant. All statistical analyses were performed with SAS software version 9.2 (SAS Institute Inc., Cary, North Carolina, USA).

**Results:** About 40.2% and 38.1% of cancer survivors and controls brushed their teeth more than 3 times a day. And 8.2% and 7.6% of cancer survivors and controls used secondary oral products. Finally, 24.9% and 23.1% of cancer survivors and controls screened oral health during the recent year. In multiple logistic regression analysis, adjusted odds ratio (aOR) for current use of secondary oral products was significantly high in cancer survivors compared to controls without cancer history (aOR = 1.30, 95% confidence interval = 1.05–1.60).

**Conclusion:** Cancer survivors reported suboptimal oral hygiene behavior. Oral health behavior excepting use of secondary oral products, was not significantly different between cancer survivor and controls. Our findings suggest that there is a significant need for increased knowledge of periodontal disease and adoption of preventive oral health behaviors that would improve oral health among cancer survivors. Furthermore, because some people with cancer do not seek regular dental care, all health care professionals should be encouraged to support efforts for more comprehensive oral health, an integral part of general health. Thus, improvement in oral health behavior among cancer survivors is essential to compensate for their higher risk of oral diseases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0490 GASTROINTESTINAL STROMAL TUMORS TREATED WITH CURATIVE INTENT

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**Introduction:** Gastrointestinal stromal tumors (GIST) are rare neoplasms of the gastrointestinal tract. In localized disease, surgical treatment is recommended, with association with tyrosine kinase inhibitors in local advanced disease. Adjuvant therapy is given according to the risk of recurrence.

**Aims & Methods:** To evaluate clinical features, type of treatment, relapse and overall survival (OS) of patients with localized GISTs. Retrospective evaluation of consecutive patients with GIST without metastatic disease followed in a single-centre outpatient clinic (2005–2015). Statistical analysis was performed with SPSS, V20 (Chi2, Fisher's exact test, Kaplan-Meier, logistic regression/AUROC).

**Results:** 96 patients were evaluated; mean age = 61 years (20–87), 56.3% female; 77% had symptoms at diagnosis, like abdominal pain (29.7%) and gastrointestinal bleeding (25.7%). Anatomic location of the tumor: stomach-52.2%, small bowel-24%, rectum-11.5%, colon-1%, extra-intestinal-5.2%, multifocal-3.1%. 92.7% (n = 89) of the patients underwent surgery (R0–89.6%). Twelve patients with advanced disease started cytoreductive treatment with imatinib, of which 3 are waiting surgery and 2 developed disease progression. All prognostic scores were effective in risk stratification: US National Institutes of Health (NIH): AUROC 0.73, modified NIH: AUROC 0.715, Armed Forces Institute of Pathology (AFIP): AUROC 0.725, Heat maps: AUROC 0.713. 24% started postoperative imatinib. Among patients with intermediate risk (NIH), 35.3% who did not start postoperative imatinib had relapse (6/17) vs 0% who received imatinib ($p = 0.015$). Among 18 patients with relapse 10 (20.2%) underwent further surgery. The overall 3- and 5-year survival rates were 93.7% and 81.7%, respectively (Kaplan-Meier).

**Conclusion:** In this study, 3-years OS was over 90% proving the excellent prognosis of localized disease. Post-operative treatment with imatinib in patients with intermediate risk was associated with absence of recurrence.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 10:30–17:00

## H. PYLORI I – POSTER EXHIBITION

## P0491 CHANGES OF INTESTINAL MICROBIOTA AFTER HELICOBACTER PYLORI ERADICATION THERAPY

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**Introduction:** Widespread use of antimicrobial agents often leads to an imbalanced composition of the intestinal microbiota. *H. pylori* eradication therapy consisting of several antimicrobial drugs also sometimes leads to adverse events, such as diarrhea. Moreover, several studies have shown that *H. pylori* infection itself may lead to shifts of the composition of the normal intestinal microflora.

**Aims & Methods:** The aim of the study was to describe the gut microbiota composition in *H. pylori*-positive and *H. pylori*-negative patients, as well as to assess the effect of eradication therapy on the composition using ''shotgun'' metagenomics.

**Results:** One hundred twenty-six stool samples were used for analysis: 58 samples from *H. pylori*-positive patients before eradication therapy, 58 - from the same patients after the completion of eradication therapy, 50 samples from *H. pylori*-negative patients (control group). Total deoxyribonucleic acid (DNA) was isolated from the stool samples using phenol extraction method and subject to whole-genome sequencing on Solid 5500 Wildfire platform. Composition of intestinal microbiota community was evaluated basing on the number of species, the qualitative composition and Shannon diversity index. In general, bacterial community in all groups was quite similar. Bacteroides, Prevotella, Eubacterium, Roseburia, Faecalibacterium and Clostridium genera were predominant in all stool samples. However, the spread in variations prevailing Firmicutes and Bacteroides phyla was wider after the treatment than in the control samples. In about half of the patients, the eradication therapy led to a decrease of both the number of species and the Shannon index indicating a decrease in the overall bacterial diversity and consequently, a reduction of the stability of community, with a possible predominance of individual species. Eradication therapy led to a reduction in the representation of the Bifidobacterium, Collinsella, Coprococcus genera, increase in the number of Clostridium, Bacteroides, Coprobacillus and Flavonifractor as well as other species. Gene-centric analysis of the functional composition in paired samples taken before and after therapy showed an increase of the relative abundance of genes conferring antibiotic resistance.

**Conclusion:** Changes in the composition of intestinal microbiota after *H. pylori* eradication therapy are individual and depend on initial condition of the intestinal microbiota. We suggest that evaluation of intestinal microflora composition prior to treatment can in the prospect predict the incidence of side effects caused by changes in microbiota composition.

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**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0492 HIGH DOSE CAM WITH VONOPRAZAN (P-CAB) PLUS AMX REGIMEN IS THE STRONGEST H. PYLORI ERADICATION TRIPLE THERAPY REGIMENS TO IMPROVE SUCCESS RATE OF CAM BASED REGIMENS

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**Introduction:** Success or failure of Amoxicillin (AMX) and Clarithromycin (CAM) based *H. pylori* (HP) eradication therapy mainly depends on sensitivity of CAM for HP. So far now, several proton pomp inhibitors (PPIs) have been used in HP eradication therapy, most of reports said that the success rate of eradication approximated from 70 to 80% on AMX and CAM-based triple therapy regardless of CAM dose (400 or 800 mg/day) in Japan. Recently the ratio of CAM resistance in Japan comes up to over 30%, we have to overcome CAM resistance using any contrivance. On the other hand, recently it is considered that the stability of continuous gastric acid suppression is one of most important factors. At the point of gastric acid suppression, we expect stronger acid suppressive drug rather than PPIs. Since Feb. 2015 we have used **P-CAB** (Potassium-Competitive Acid Blocker) instead of PPIs in AMX and CAM-based HP eradication therapy to improve success rate.
**Aims & Methods:** The aim of this study is to elucidate effects of CAM dose on success rate of **P-CAB** Vonoprazan (VPZ) and one of PPI Rabeprazol (RPZ) based triple therapy regimens (VAC, RAC). This study is a single-center, prospective case study from Jan. 2012 to Oct. 2015. A total of 648 patients (HP positive) were enrolled. Mean age of patients was 54.4 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 CAM (400 or 800 mg/day) b.i.d. for 7 days. Regimen of RAC (400 or 800) was RPZ (20 mg/day) b.i.d., AMX (1, 500 mg/day) b.i.d. plus CAM (400 or 800 mg/day) b.i.d. for 7 days. The judgement of success or failure on eradication was done with urea breath test on 3 months later after eradication therapy to avoid false negative results.
**Results:** Success rate of VAC 800 showed significantly high (90/92 = 97.8%, PPT) rather than VAC 400 (98/113 = 86.7%, PPT). The average success rate of VAC regimens was 91.7% (188/205, PPT). On the other hand, success rate of RAC 800 showed significantly high (190/245 = 77.6%, PPT) rather than RAC 400 (140/198 = 70.7%, PPT). The average success rate of RAC regimens was 74.5% (330/443, PPT). Success rate of high dose CAM regimens (VAC 800 and RAC 800) were significantly higher than standard dose CAM 400 regimens ($p < 0.05$). These results suggest that using high dose CAM with Vonoprazan (P-CAB) plus AMX regimen might be the strongest *H. pylori* eradication triple therapy regimens to overcome CAM resistance.
**Conclusion:** In case of AMX, CAM and P-CAB based triple therapy regimens, we cloud be able to expect significantly high success rate of HP eradication. This regimen might be expected to improve success rate even if CAM resistance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0493 EFFICACY OF VONOPRAZAN BASED NEW HELICOBACTER PYLORI ERADICATION THERAPY

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**Introduction:** It is widely known that *Helicobacter pylori* (*H. pylori*) causes several diseases such as gastric cancers and gastroduodenal ulcer disease. Previous reports showed that *H. pylori* eradication therapy prevent recurrence of gastroduodenal ulcer or metachronous gastric carcinoma. The *H. pylori* eradication therapies with proton pump inhibitors (PPIs) are, today, widely given, but the eradication rates are not sufficient due to increase of resistant bacteria or insufficient suppression of gastric acid with PPIs. A new potassium competitive acid blocker, Vonoprazan (VPZ) has been recently developed which suppresses acid secretion more potently than PPIs. A latest clinical trial showed that the eradication rate of new anti-*H. pylori* regimen with VPZ was higher than that of a conventional *H. pylori* eradication therapy using a PPI, Lansoprazole (LPZ) (Murakami et al. Gut 2016). However, its eradication rate in clinical site and comparison with that of other PPIs are not elucidated.
**Aims & Methods:** The purpose of this study is to evaluate the efficacy of VPZ combined regimen against *H. pylori* in clinical practice. We retrospectively analyzed eradication rates of *H. pylori* positive 525 patients whom we prescribed VPZ, LPZ and Rabeprazole (RPZ) based triplet therapy from August 2014 to February 2016. Those cases include 390 cases of first line therapies; 155 cases of VPZ based first line therapy (VPZ 20 mg+Amoxiciline (AMX) 750 mg+Cratithromycine (CLR) 200 mg×7days (7 d), with all drugs given twice daily: VAC); 157 cases of LPZ based first line therapy (LPZ 30 mg+AMX 750 mg+CLR 200 mg×7d, with all drugs given twice daily: LAC); and 78 cases of RPZ based first line therapy (RPZ 10 mg+AMX 750 mg+CLR 200 mg×7d, with all drugs given twice daily: RAC). 92 patients received metronidazole (MTZ) combined second line therapy, including 30 cases of VPZ based therapy (VPZ 20 mg+AMX 750 mg+MTZ 250 mg×7d, with all drugs given twice daily: VAM); 14 cases of LPZ based therapy (LPZ 30 mg+AMX 750 mg+MTZ 250 mg×7d, with all drugs given twice daily: LAM), and 48 cases of RPZ based therapy (RPZ 10 mg+AMX 750 mg+MTZ 250 mg×7d, with all drugs given twice daily: RAM). The remaining 43 cases were excluded due to neither first line nor second line therapy, or different drug dose. The eradication rates and the incidences of drug adverse effects in those therapies were calculated. Subgroup analyses were performed to investigate the patients' backgrounds affecting the efficacy of those therapies. Statistical analyses were performed with chi-squared test.
**Results:** The *H. pylori* eradication rate with VAC in first line therapy were 82.2%, which was significantly higher than that with LAC (68.1%, $p = 0.0067$), and with RAC (61.4%, $p = 0.0013$). The incidences of drug adverse effects with VAC, LAC, and RAC were 5.9%, 4.3%, and 4.3%, respectively. There were no significant differences regarding incidences of adverse events, body mass index, and the proportion of atrophic gastritis, and the prevalence of gastroduodenal ulcers and gastric cancer among those three therapies. The second line eradication rate with VAM, LAM and RAM were 92.3%, 85.7% and 84.1%, and there were no significant difference.
**Conclusion:** The present study demonstrates that the new *H. pylori* eradication first line therapy in combination with VPZ is superior to the conventional ones with LPZ and RPZ. VPZ based second line therapy also showed higher eradication rate compared with RPZ and LPZ.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0494 HIGH-DOSE ONE-WEEK TRIPLE THERAPY FOR H.PYLORI INFECTION

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**Introduction:** Eradication of *H. pylori* infection cures duodenal ulcer disease; since our original report of a one week eradication regime[1], widespread use of eradication therapy for other indications and increasing prevalence of antibiotic resistance has resulted in efficacy of <75% for standard one week regimes[2], leading to more complex sequential, quadruple and hybrid treatment regimes[3].
**Aims & Methods:** This prospective observational cohort study aims to evaluate the efficacy of a high dose one week triple therapy regime. Patients undergoing OGD and found to be infected with *H. pylori* by CLO-test were considered for inclusion. Clinical data was extracted by review of electronic case notes. All patients were treated with omeprazole 20 mg bd, clarithromycin 500 mg tds and metronidazole 400 mg tds for 1 week by a single prescriber (RL) immediately after the end of the procedure. All patients were advised about possible side-effects and the importance of compliance in ensuring successful eradication. *H. pylori* status was confirmed prior to treatment by CLO-test +/- antral and corpus histology. Eradication was assessed by $^{13}$C-Urea Breath Test ($^{13}$C-UBT) at least 6 weeks after the end of treatment.
**Results:** From 2013–2016, ninety-three patients (male, n = 60 (65%), mean age 55 yr, range 22–76yrs) with evidence of peptic ulcer disease (n = 76 (82%)) severe oesophagitis (n = 4, (4%)) or other indication for treatment were endoscoped and found to be *H. pylori* positive. Patients were mainly Caucasian (46%) or Afro-Caribbean (34%), and non-smokers (76%). Six patients had previously received *H. pylori* eradication therapy from their GP, but remained infected. Seventeen patients did not attend for their follow-up $^{13}$C-UBT. In previously untreated patients, eradication of *H. pylori* was achieved in 67/70 (96% [95% CI 91–100%] and also in 4/6 (67%) of patients previously treated by their GP.
**Conclusion:** A high dose one week *H. pylori* eradication regime might be an alternative to current more complex lengthy treatment options, but with the advantage of maximizing the opportunity for patient compliance particularly for patients with *H. pylori* associated ulcer disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0495 THE EFFECTIVENESS OF VONOPRAZAN-BASED H.PYLORI ERADICATION THERAPY IN OUR HOSPITAL

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**Introduction:** Vonoprazan (P-cab) is a novel oral potassium-competitive acid blocker, which overcomes the weaknesses of proton pump inhibitor (PPI). Unlike previous PPIs, P-cab inhibits the enzyme in a K+-competitive and reversible manner. P-cab is shown to accumulate in parietal cells with its acid-inhibitory effects as well as greater increases in gastric pH than previous PPIs as it accumulated in high concentrations and became slowly cleared from gastric glands. Therefore, P-cab is promising drug for *H. pylori* eradication therapy.
**Aims & Methods:** The aim of this study is to evaluate the effectiveness of P-cab based *H. pylori* eradication therapy compared with previous PPI based triple therapy. We treated with previous PPIs based eradication therapy from May 2012 to May 2015 and the P-cab based eradication therapy between June 2015 and February 2016. *H. pylori* eradication therapies were as follows; 1st line therapies were PPIs or P-cab, amoxicillin (AMPC), clarithromycin (CAM), 2nd line therapies were PPI or P-cab, metronidazole (MNZ), AMPC, 3rd line therapies were PPI or P-cab, AMPC, MNZ, ecabet sodium for 2 weeks, Penicillin allergy therapies were PPI or P-cab, minocycline (MINO), MNZ. We compared with eradication rates, completion rates, and adverse reaction rates between previous PPIs based eradication therapy and P-cab based eradication therapy. The *H. pylori* eradication was diagnosed based on the $^{13}$C-urea breath test performed 12 weeks after completion of the eradication therapy. Completion was defined to finish taking all medicines of these therapies.
**Results:** We enrolled 398 patients (Age Mean±SD: 61.3 years ± 11.8, Male/Female: 182/216) who treated with PPI based therapy, and 69 patients (Age Mean±SD 57.7 years±11.4, Male/Female: 39/30) who treated with P-cab based therapy in this study. Overall eradication rate was 94.2% (65/69) in the P-cab group vs 79.4% (316/398) in the PPI group ($p = 0.002$). Completion rate and adverse reaction rate were 100% (69/69) and 7.2% (5/69) in the P-cab group compared with 98% (390/398) and 4.0% (16/398) in the PPI group. The eradication rate of 1st line therapy was 92.1% (36/41) with P-cab vs 76.7% (214/279) with PPI, completion rate 100% (41/41) vs 98.2% (274/279), adverse reaction rate 2.6% (1/41) vs 2.9% (8/279). The eradication rate of 2nd line therapy was 100% (11/11) with P-cab versus 86.7% (65/75) with PPI, completion rate 100% (11/11) vs 98.7% (74/75), adverse reaction rate 0% (0/11) vs 5.3% (2/75). The eradication rate of 3rd line therapy was 80% (8/10) with P-cab versus 72% (18/25) with PPI, completion rate 100% (10/10) vs 92.0% (23/25), adverse reaction rate 40% (4/10) vs 20% (5/25). The eradication rate of penicillin allergy therapy was 100% (7/7) with P-cab vs 100% (19/19) with PPI, completion rate 100% (7/7) vs 100% (19/19), adverse reaction rate 0% (0/7) vs 5.3% (1/19).Most common adverse reaction of P-cab was diarrhea.
**Conclusion:** P-cab based *H. pylori* eradication therapy is more effective than previous PPI based *H. pylori* eradication therapy in 1st, 2nd and 3rd lines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0496 EFFICACY OF RIFABUTIN-BASED TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION AS A RESCUE THERAPY

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**Introduction:** With the rising prevalence of antimicrobial resistance, the treatment success of *Helicobacter pylori* eradication has recently declined. The Maastricht IV/Florence consensus report recommends that culture and antimicrobial sensitivity testing should be performed after one or two treatment failures with different antibiotics. Rifabutin-based triple therapy has been applied as a rescue treatment.
**Aims & Methods:** The aim of the present study was to evaluate the efficacy of rifabutin-based triple therapy for *Helicobacter pylori* eradication as a rescue therapy. Patients who experienced twice *Helicobacter pylori* eradication failure were treated with esomeprazole 40 mg twice daily, rifabutin 150 mg twice daily and amoxicillin 1 g twice daily for 7 days. Eradication status was determined by the 13 C-urea breath test performed 4 weeks later. Antibiotic susceptibility was determined by the E-test from *Helicobacter pylori* culture and real-time PCR for DNA sequencing from gastric biopsy specimens. Clarithromycin and levofloxacin phenotypic resistance were defined as a minimum inhibitory concentration (MIC) of 1 μg/mL or more. Mutations in *Helicobacter pylori* 23 S rRNA and gyrA genes associated with resistance to clarithromycin and levofloxacin, respectively, were determined, too.
**Results:** Total 33 patients were enrolled. All of them complete treatment course and had follow-up 13 C-urea breath test. The successful eradication rate was 72.2% (24/33). Antibiotic susceptibility was determined in these patients and 22 of them had clarithromycin and levofloxacin dual resistant *Helicobacter pylori* strains. The successful eradication rate was 81.8% (18/22) in patients with dual resistant strains. Another 10 days course of rifabutin-base triple therapy was prescribed for two failure subjects and one of them had successful *Helicobacter pylori* eradication.
**Conclusion:** The present study suggests that rifabutin-based triple therapy can be used for *Helicobacter pylori* eradication in clarithromycin and levofloxacin dual resistant strains.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0497 EFFICACY OF 7-DAY BISMUTH-BASED QUADRUPLE THERAPY VERSUS 14-DAY MOXIFLOXACIN-BASED TRIPLE THERAPY FOR SECOND-LINE TREATMENT OF HELICOBACTER PYLORI INFECTION

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**Introduction:** Moxifloxacin-based triple therapy has been suggested as second-line eradication therapy for *Helicobacter pylori* (*H. pylori*) infection.
**Aims & Methods:** The aims of this study were to evaluate the efficacy of 14-day moxifloxacin-based triple therapy in second-line *H. pylori* eradication comparing to 7-day bismuth-based quadruple therapy. From January 2011 to December 2015, a total of 569 patients who were failed to first-line triple therapy and received 7-day bismuth-based quadruple therapy or 14-day moxifloxacin-based triple therapy were retrospectively enrolled. 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 $^{13}$C-urea breath test or a rapid urease test at least 4 weeks after the completion of eradication therapy.
**Results:** Total of 487 and 82 patients received the 7-day bismuth-based quadruple therapy and 14-day moxifloxacin-based triple therapy, respectively. ITT eradication rates were 75.4% (367/487; 95% confidential interval (CI), 70.8%-79.3%) in the 7-day bismuth-based quadruple therapy group and 58.5% (48/82; 95% CI, 46.2%-70.8%) in the 14-day moxifloxacin-based triple therapy group ($P = 0.003$). And, PP eradication rates were 93.6% (366/391; 95% CI, 91.0%-95.9%) in the 7-day bismuth-based quadruple therapy group and 73.8% (48/65; 95% CI: 63.1%-84.6%) in the 14-day moxifloxacin-based triple therapy group ($P < 0.001$). The eradication rates in the 7-day bismuth-based quadruple therapy group were significantly higher than in the 14-day moxifloxacin-based triple therapy group according to both ITT and PP analyses. Adverse event rates were 17.1% (67/391) in the 7-day bismuth-based quadruple therapy group and 7.7% (5/65) in the 14-day moxifloxacin-based triple therapy group ($P = 0.065$).
**Conclusion:** The 7-day bismuth-based quadruple therapy is still an effective second-line therapy in patients who failed the first-line triple therapy considering the high resistance of antibiotics in Korea.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0498 CLINICOPATHOLOGICAL FEATURES OF HELICOBACTER PYLORI-NEGATIVE EARLY GASTRIC CANCER

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**Introduction:** *Helicobacter pylori* (Hp) infection has been well recognized as a major risk for gastric cancer, and most patients with gastric cancer are infected with Hp. Recently, several studies showed the existence of a small number of Hp-negative gastric cancers (HPNGC) [1, 2]. However, results were not consistent and controversy exists regarding the clinicopathological features of HPNGC.
**Aims & Methods:** This study aimed to evaluate the clinicopathological features of HPNGC compared to Hp-positive gastric cancer (HPPGC). We retrospectively analyzed 426 cases of early gastric cancer that underwent endoscopic resection at our hospital from April 2009 to January 2016. Twenty-three HPNGC cases (11 males, 12 females; mean age 62.3 y; 24 lesions) and 174 HPPGC cases except for those with past infection (151 males, 41 females; mean age 70.4 y; 192 lesions) were enrolled in this study. Hp-negative status was defined as the fulfillment of all of the following criteria: no eradication history, no mucosal atrophy in endoscopic (C-0 or 1, according to Kimura-Takemoto classification) and pathological findings, negative rapid urease test or urease breath test, serum Hp-immunoglobulin G test, or stool antigen.
**Results:** Prevalence of HPNGC was calculated as 5.4%. No significant difference was observed in macroscopic types, median depth of submucosal (SM) invasion, and the curative resection rate. There were significant differences (HPNGC vs. HPPGC) in mean age (62.3 y vs. 70.4 y, $P < 0.01$), gender (male/female = 11/12 vs. 151/41, $P < 0.01$), and tumor size ($9 \pm 4.2$ vs. $23.7 \pm 8.7$ mm, $P < 0.01$). Regarding tumor location, HPNGC was observed more often at the upper third of the stomach than HPPGC (cardia/U/M/L = 1/13/4/6 vs. 5/11/91/85, $P < 0.01$). Histologically, gastric adenocarcinoma of fundic gland type (GAFG) was observed significantly more often in HPNGC than HPPGC (58.3% vs. 0%, $P < 0.01$). There were significant differences (HPNGC vs. HPPGC) in SM invasion rate (50% vs. 11.9%, $P < 0.01$) and lymphatic and venous invasion rate (0% vs. 5.4%, $P < 0.01$).

In HPNGC, frequency according to histological type was as follows: GAFG/well-differentiated adenocarcinoma (WDA)/signet-ring cell carcinoma (Sig) = 14 (58.3%)/7 (29.2%)/3 (12.5%). GAFG tended to be observed at the upper third of the stomach (cardia/U/M/L = 0/12/2/0, $P < 0.01$) while WDA tended to be observed at the lower third of the stomach (cardia/U/M/L = 1/1/0/5, $P < 0.01$) and Sig tended to be observed at middle third of the stomach (cardia/U/M/L = 0/0/2/1, $P < 0.01$).

**Conclusion:** HPNGC is very rare but has distinct clinicopathological features, especially in terms of age, sex, size of tumor, tumor location, histological type, and low grade malignancy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0499 IMPLEMENTATION OF A CLINICAL-ENDOSCOPIC-PATHOLOGICAL -INDEX (CEPIX) FOR ESTIMATING THE RISK OF SPORADIC NON-CARDIA GASTRIC CARCINOMA IN DYSPECTIC PATIENTS AND GASTRITIS ASSOCIATED WITH INFECTION BY HELICOBACTER PYLORI IN A CLINICAL SETTING. A PROPOSAL


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**Introduction:** Gastric cancer still represents a major healthcare issue; in fact, gastric malignancies are mostly diagnosed in their advanced stage, and are associated to high mortality rates. Etiologically, sporadic gastric cancer is considered a multifactorial disease. Environmental or lifestyle factors are major contributors to the etiology. *Helicobacter pylori* infection (the major oncogenic agent), age, geographic localization, gender, ethnic group, high intake of salty and smoked food, low consumption of fruits and vegetables, alcohol consumption, cigarette smoking, family history of cancer, genetics factors, some occupations, low socioeconomic status, physical activity, radiation, statins and non-steroidal anti-inflammatory drugs use, appear contribute in greater or lesser degree to gastric carcinogenesis. Some of these risk factors are well known, whereas others show no clear links. Rugge et al point out that categorizing patients in terms of their risk of developing gastric cancer should enable clinicians to provide the most appropriate patient care and it is important stratify risk in terms of reversibility or stabilization of carcinogenesis process.

**Aims & Methods:** In the clinical setting is mandatory the need to estimate the risk of developing gastric cancer in patients with gastritis associated with *Helicobacter pylori* infection. Therefore, we propose the implementation of a Clinical-Endoscopic-Pathological -Index (CEPIx). CEPIx was applied to patients with dyspeptic disease and gastritis associated with *Helicobacter pylori* infection and without *Helicobacter pylori* infection. The CEPIx includes clinical aspects (age, family history of cancer, smoking history, geographic particularities, ethnic group, dietary factors, helminths co-infection), endoscopic aspects (presence of gastric ulcer) and pathological aspects (phenotype and topography of gastritis). Sixty five patients with dyspeptic disease were studied at Gastroenterology Department of Universitary Hospital of Maracaibo, Venezuela. Forty six with gastritis associated with *Helicobacter pylori* infection and nineteen without *Helicobacter pylori* infection.

**Results:** Dyspeptic patients with gastritis associated with *Helicobacter pylori* infection displays higher general score, exhibits higher mean age, family cancer history, a more conspicuous and frequent smoking habit, higher mean score in clinical and pathological aspects, compared with dyspeptic patients without *Helicobacter pylori* infection.

**Conclusion:** The implementation of a Clinical-Endoscopic-Pathological-Index for estimating the risk of sporadic non-cardia gastric carcinoma in dyspectic patients and gastritis associated with infection by *Helicobacter pylori* in a clinical setting could be a very useful tool for a more precise and individual estimation of the risk for gastric cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0500 USEFULNESS OF THE MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING FOR THE DETECTION OF TUMOR DEMARCATION IN EARLY GASTRIC CANCERS AFTER HELICOBACTER PYLORI ERADICATION


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**Introduction:** The recent results of a randomized controlled study and meta-analysis study have demonstrated that *Helicobacter pylori* (Hp) eradication reduces the development of gastric cancer. However, gastric cancers may still occur following successful Hp eradication. Therefore, it is important to determine the clinicopathological features of early gastric cancers after Hp eradication. Several previous studies reported that gastric cancers developing after Hp eradication display unclear demarcation in approximately 24–40% of lesions [1] [2]. However, the role of magnifying endoscopy with narrow-band imaging (ME-NBI) using the VS classification system (VSCS) has not been evaluated in tumor demarcation detection.

**Aims & Methods:** The aim of this study was to assess the clinicopathological features of early gastric cancers after Hp eradication by comparing lesions with Hp positive early gastric cancer. Additionally, we analyzed the usefulness of ME-NBI using VSCS for the detection of tumor demarcation. There were 239 patients with early gastric cancer who underwent endoscopic resection in our hospital between April 2013 and March 2016. We excluded the following cases: undifferentiated or mixed-type gastric cancer (15), special type gastric cancer (24), and cases with an unknown eradication history (96). We enrolled 34 Hp eradicated patients (28 males, 6 females; mean age 71.6 y) and 70 Hp positive patients (54 males, 16 females; mean age 72.6 y). We then evaluated tumor demarcation, using a classification system. All DL (+) tumors were defined as having a clear demarcation line present circumferentially between the lesion and non-lesion areas. The DL (-) tumors had an absent or unclear demarcation line. We then analyzed the frequency of DL (-) cases in each patient populations.

**Results:** There were no significant differences between patient groups for the following characteristics: mean age, gender, operative method, tumor location, extent of atrophic gastritis, main histological type, invasion depth, and curative resection rate. However, there were significant differences (Hp eradicated group vs. Hp positive group) in macroscopic type (elevated/flat/depressed = 9/0/25 vs. 35/1/34, $P < 0.05$), and tumor size ($11.4 \pm 13.4$ vs. $16.2 \pm 23.1$ mm, $P < 0.05$). Our analysis of tumor demarcation by ME-NBI using VSCS indicated that DL (-) cases were significantly higher in the Hp eradicated group than in the Hp positive group (11.8% (4 (absent:1, unclear:3)/34) vs. 1.4% (1 (absent:0, unclear:1)/70), $P < 0.01$). The histopathological analysis of the four DL (-) cases in the Hp eradicated group were composed of cancers with low-grade atypia or mixed with non-neoplastic epithelium in the demarcation area. The demarcation line might become unclear as a result of these findings. However, we could detect clear tumor demarcation in 88.2% of Hp eradicated cases using ME-NBI. We estimated the border between the lesion and non-lesion areas based on subtle changes of micro-vascular/surface pattern with ME-NBI in the 4 DL unclear cases. There were no cases of positive lateral margins in the DL (-) Hp eradicated group.

**Conclusion:** Several studies have reported that tumor demarcation tends to be unclear in gastric cancers developing after Hp eradication. Our results show that ME-NBI using VSCS may detect tumor demarcation in gastric cancers after Hp eradication.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0501 THE IMPACT OF HELICOBACTER PYLORI INFECTION ON THE RISK OF ADVANCED COLORECTAL NEOPLASM IS DIFFERENT BY AGE GROUP


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**Introduction:** Whether *Helicobacter pylori* (HP) infection affects the risk of advanced colorectal neoplasm (ACN) regardless of aging remain uncertain.

**Abstract No: P0501**

**Table 1:** Multivariable analyses for advanced colorectal neoplasm in patients with different age groups.

| Variables | All age HR | 95% CI | P | Age <50 years HR | 95% CI | P | Age ≥50 years HR | 95% CI | P |
|---|---|---|---|---|---|---|---|---|---|
| Age, years, mean (range) | 1.058 | 1.050–1.066 | <0.001 | 1.117 | 1.080–1.155 | <0.001 | 1.056 | 1.043–1.070 | <0.001 |
| BMI ≥23 kg/m$^2$ | 1.151 | 0.948–1.399 | 0.155 | 1.060 | 0.740–1.517 | 0.752 | 1.199 | 0.949–1.515 | 0.129 |
| Abdominal obesity | 0.940 | 0.738–1.196 | 0.613 | 0.891 | 0.573–1.386 | 0.610 | 0.872 | 0.652–1.168 | 0.359 |
| Male gender | 1.316 | 1.030–1.682 | 0.028 | 1.551 | 0.961–2.502 | 0.072 | 1.301 | 0.971–1.744 | 0.078 |
| HP infection | 1.153 | 0.981–1.354 | 0.083 | 1.468 | 1.094–1.969 | 0.011 | 1.021 | 0.842–1.238 | 0.834 |
| Smoking history | 1.500 | 1.219–1.846 | <0.001 | 1.663 | 1.142–2.420 | 0.008 | 1.426 | 1.109–1.834 | 0.006 |
| DM | 1.333 | 1.008–1.763 | 0.044 | 1.279 | 0.702–2.328 | 0.421 | 1.356 | 0.989–1.861 | 0.059 |
| HDL <40 mg/dL | 0.904 | 0.738–1.108 | 0.332 | 0.966 | 0.661–1.410 | 0.857 | 0.867 | 0.682–1.102 | 0.244 |
| TG ≥200 mg/dL | 1.193 | 0.952–1.495 | 0.125 | 1.441 | 0.999–2.079 | 0.050 | 1.043 | 0.781–1.394 | 0.775 |

HR, hazard ratio; CI, confidence interval; BMI, body mass index; HP, Helicobacter pylori; DM, diabetes mellitus; GGT, gamma-glutamyl transpeptidase; HDL, high-density lipoprotein; TG, triglyceride.

**Aims & Methods:** This retrospective study investigated the association between HP infection and ACN in different age groups with medical records of patients who underwent a general medical examination, including colonoscopy for the first time at the Gangnam Severance hospital, Seoul, Korea. The patients with previous history of colorectal cancer were excluded. ACN was defined as the presence of colorectal cancer or at least one colorectal adenoma with at least one of the following features: ≥1 cm in size, tubulovillous or villous adenoma or high grade dysplasia. The presence of ACN was determined by reports of colonoscopy and pathology. HP infection was determined by the presence of serum anti-HP immunoglobulin G (IgG). In case of the titer of anti-HP IgG was reportedly in the borderline range, the results of the rapid urease test, if present, were alternatively adopted. Abdominal obesity was defined as waist-hip ratio above 0.9 for males and above 0.85 for females. Univariable analyses with continuous and nominal variables were performed using Student's t-test and Fisher's exact test, respectively. Multivariable analyses were performed using a binary logistic regression test.

**Results:** A total of 21, 125 patients (11, 987 male and 9, 138 female) was studied. Mean age was 49.64 years (range, 18–91 years). Among those, ACA was reported in 728 patients (3.4%). In univariable analyses, older age (mean 55.62 years [range, 31–86 years] vs. 49.43 years [range, 18–91 years] in patients with and without ACN, respectively; p <0.001), body mass index ≥23 kg/m$^2$ (64.0% vs. 55.1%; p <0.001), HP infection (60.7% vs. 56.0%; p = 0.018), male gender (69.8% vs. 56.3%; p <0.001), presence of abdominal obesity (69.4% vs. 51.8%; p <0.001), smoking history (62.2% vs. 49.1%; p <0.001), diabetes mellitus (DM) (9.2% vs. 5.3%, p <0.001), high-density lipoprotein <40 mg/dL (20.1% vs. 15.4%; p = 0.001) and triglyceride ≥200 mg/dL (16.6% vs. 12.2%; p = 0.001) were significantly associated with increasing risk of ACN. Alcohol intake (p = 0.271), hypertension (p = 0.173), use of aspirin (p = 0.667) or non-steroidal anti-inflammatory drugs (p = 0.197), family history of colorectal cancer (p = 0.448) and low-density lipoprotein ≥100 mg/dL (p = 0.820) were not significant. In multivariable analyses, older age (hazard ratio [HR], 1.058; p <0.001), male gender (HR, 1.316; p = 0.028), presence of smoking history (HR, 1.489; p <0.001) and DM (HR, 1.333; p = 0.044) showed independent significance in all age group (Table 1). In subgroup analyses, HP infection was significant only in patients with age <50 years (Table 1).

**Conclusion:** Our data suggest that HP infection is associated with increasing risk of ACN in patients with age <50 years. Older age, male gender, presence of smoking history and DM were significant risk factors for ACN in all age group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0502 LONG-TERM FOLLOW UP OF PEPSINOGEN I/II RATIO AFTER HELICOBACTER PYLORI ERADICATION

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**Introduction:** Although several studies regarding short term follow-up of pepsinogen I/II (PG I/II) after *H. pylori* eradication suggested recovery to normal range, long term follow-up of PG I/II is few. We evaluated the serial long-term follow-up of PG I/II.

**Aims & Methods:** Between 2007 and 2014, a total of 773 patients with gastric cancer who underwent endoscopic resection, pepsinogen test, and *H. pylori* test at baseline were enrolled. *H. pylori* eradication therapy was provided after endoscopic resection if *H. pylori* was present. Serial endoscopic and pepsinogen test were performed every year after resection. Study group was classified into non-infected group, eradication group, and non-eradication group. Low PG I/II was defined as ≤3.

**Results:** PG I/II ratio was higher in non-infected patients with *H. pylori* (n = 275, 4.99) than infected patients (n = 498, 3.53) (P < 0.05). After *H. pylori* eradication, PG I/II increased from 3.55 at diagnosis to 5.81 at 1 yr and 5.63 at 2 yr (each P < 0.05), respectively. Follow-up PG I/II is similar with that of baseline in non-infected group. However, PG I/II was 3.48 at diagnosis, 3.94 at 1year, and 2.75 at 2year in non-eradication group. The adjusted OR for low PG I/II in non-eradication group comparing to eradication group was 4.78 (95% CI 2.15–10.67) at 1 yr and 8.13 (95% CI 2.56–25.83) at 2 yr.

**Conclusion:** PG I/II was definitely low in *H. pylori* infected subjects comparing to *H. pylori* non-infected patients. After *H. pylori* eradication, PG I/II was recovered up to the level of non-infected patients and the recovered PG I/II maintained.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0503 PERSISTENT HELICOBACTER PYLORI INFECTION AND OLD AGE ARE RISK FACTORS FOR METACHRONOUS RECURRENCE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION OF EARLY GASTRIC CANCER

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**Introduction:** Although endoscopic submucosal dissection (ESD) is widely accepted as curative treatment method for early gastric cacner (EGC) worldwide, metachronous recurrence often occurs after endoscopic submucosal dissection for early gastric cancer. But, there is insufficient data about the role of *Helicobacter pylori* (*H. pylori*) infection and other risk factors for recurrence.

**Aims & Methods:** We aimed to compare the metachronous lesion in the *H. pylori* persistent group and the negative group and to identify risk factors for metachronous lesion. We retrospectively analyzed 782 patients who underwent ESD for between January 2008 and December 2013. We excluded patients with dysplasia or patients not tested for *H. pylori* infection. Patients were classified into the persistent group (n = 18) or negative group (n = 167) and the follow-up data were analyzed retrospectively.

**Results:** A total 185 patients were enrolled. Successful eradication was achieved in 167 patients (90.2%). At 61.1 months' median follow up, metachronous recurrence was diagnosed in 24 patients (12.9%), including 12 cancers and 12 dysplasias. The incidence of metachronous gastric lesions developed more in >70 year-old group (p = 0.021) and *H. pylori* persistent (non-eradicated or failed) group (p = 0.006).

**Conclusion:** *H. pylori* infection and old age were independent risk factor for metachronous gastric lesions after ESD in early gastric cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0504 CLINICOPATHOLOGICAL CHARACTERISTICS OF GASTRIC CANCER DETECTED AFTER SUCCESSFUL HELICOBACTER PYLORI ERADICATION

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**Introduction:** Although successful eradication of *Helicobacter pylori* (HP) will decrease the risk of gastric cancer (GC), characteristics of GC that is detected after HP eradication is not fully known.

**Aims & Methods:** The aim of this study is to clarify clinicopathological characteristics of GC detected in patients after successful HP eradication. Among 888 patients who were diagnosed as GC during April to December 2015, those who had undergone successful HP eradication at least one year before were extracted. Patients who had less than 3 years after HP eradication until the diagnosis of GC were classified as early group, those who had more than 3 years were classified as late group. The clinicopathological characteristics of GC among the early and late groups were compared. Patients with a remnant stomach, those who had unsuccessful HP eradication were excluded.
**Results:** A total of 101 lesions in 79 patients (58 men) with a median age of 70 (range 27 to 89) were extracted. The reason for HP eradiation was gastritis (57%), gastric ulcer (23%) and endoscopic resection for early GC (14%). The median interval from HP eradication to the diagnosis of GC was 3 years (range 1 to 22). The location of the lesions was in the middle or lower stomach in 77% of cases. The median diameter of the lesion was 16 mm (range 2 to 235), 83% were of the differentiated type, and 10 lesions were advanced GC. Fifty lesions were detected in 37 patients in the early group. Most of the patients had extensive atrophic gastritis (78%), the lesions were red or isocolor (90%), and the pathological depth was pT1a in 80% of the lesions. Fifty-one lesions were detected in 42 patients in the late group. Half of the patients had extensive atrophic gastritis (52%), the ratio of pale-colored lesions increased (26%), and 38% of the lesions were deeper than pT1b. The number of patients receiving periodical endoscopy every one or two years was significantly larger among the early group. There were no significant differences in lesion size, location, macroscopic type and histology between the groups.
**Conclusion:** Significant difference was observed among the degree of atrophic gastritis, the color and depth of GC detected in early and late phase after HP eradication. More advanced lesions were detected in the late phase suggesting the importance of periodic surveillance after HP eradication.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0505 DOWN-REGULATION OF LNCRNA NR_033122 REPRESSES VPS11 EXPRESSION BY EPIGENETIC MODULATION IN H. PYLORI-RELATED GASTRIC CARCINOMA

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**Introduction:** Long non-coding RNAs (lncRNAs) have been identified as key molecular players in the regulation of gene expression in multiple carcinogenic processes. They are involved in epigenetic modulation by recruiting DNA methyltransferases to promoter of certain genes. Some of these genes are supposed to be related to tumorigenesis. Although *Helicobacter pylori* is assumed to play a pathophysiological role in gastric carcinoma, little is known about its impact on the interaction between lncRNA and DNA methylation.
**Aims & Methods:** Based on comprehensive lncRNA microarray and Methylation BeadChip for Hp-related gastric cancer sample, we found lncRNA NR_033122 and VPS11 to be close in chromosome 11. Real-time PCR was used to measure level of lncRNA NR_033122 and VPS11 in 32 gastric cancer and paired adjacent nontumor tissue samples. The methylation level of VPS11 was determined by bisulfite sequencing PCR. lncRNAs and VPS11 were transferred by lentiviral vectors or down regulated with si-RNAs in MGC-803, SGC-7901 and AGS. The interaction between lncRNA NR_033122 and VPS11 was detected by RNA pulldown, RIP and ChIp.
**Results:** Expression level of lncRNA NR_033122 and VPS11 were significantly lower in Hp-related GC than neighboured nontumor tissues. Three-dimensional contours showed a relationship between NR_033122 expression, and VPS11 expression and VPS11 methylation. In ChIp assays, NR_033122 was associated with NF-KB p65, activation of which could recruit DNMT. Overexpression of NR_033122 in 3 cell lines attenuated their proliferation and ability to form colonies, and reduced the expression of VPS11, whereas down regulation of NR_033122 increased the levels of VPS11. CpG islands in POU3F3 were densely hypermethylated in cell lines after Hp stimulation. Pharmacologic inhibition of p65 increased the levels of VPS11 and significantly reduced binding of DNMT to its promoter.
**Conclusion:** lncRNA NR_033122 decreased after *H. pylori* infection and subsequent activation of NF-$\kappa$B p65 recruited DNMT, which led to VPS11 promoter methylation. Both lncRNA NR_033122 and VPS11 are potential tumor suppressors in gastric cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0506 LINE-1 HYPOMETHYLATION IS A RARE EVENT IN PRENEOPLASTIC STAGES OF GASTRIC CARCINOGENESIS

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**Introduction:** LINE-1 methylation is an established marker for assessment of diffuse genomic DNA methylation, which is a frequent event in carcinogenesis. The alterations in LINE-1 methylation have been suggested for gastric cancer (GC) while the data to premalignant gastric lesions remain poorly reported. The aim of the study was to evaluate the LINE-1 methylation status at different stages of gastric carcinogenesis and evaluate its prognostic potential.
**Aims & Methods:** LINE-1 methylation was analyzed in 267 tissue samples by bisulfite pyrosequencing. Overall, the study included 80 pairs of primary gastric cancer tissues (T-GC) with corresponding adjacent normal gastric mucosa (N-GC), 24 pairs of primary colorectal cancer (CRC) tissues (T-CRC) with corresponding normal mucosa (N-CRC), 19 gastric tissues from controls (N), 37 tissues from patients with chronic non-atrophic and atrophic gastritis (CG). Survival analysis was performed using Kaplan-Meier curves.
**Results:** LINE-1 methylation level was lower in both GC and CRC tumor tissues when compared to paired healthy adjacent tissues. No difference was observed for LINE-1 methylation status between patients with normal gastric mucosa, CG and N-GC. LINE-1 methylation showed no correlation between N-GC and T-GC while tended to correlate with age of the patients at the diagnosis. Subgroup stratification analysis did not reveal significant differences in LINE-1 methylation status according to tumor stage, anatomical location, histological subtype, differentiation grade or *Helicobacter pylori* status. In our cohort, we observed similar survival data between patients with high or low LINE-1 methylation.
**Conclusion:** LINE-1 hypomethylation is characteristic feature in GC tissues; however, it seems to be a rare event in early stages of gastric carcinogenesis such as preneoplastic conditions. In our population, we could not confirm the prognostic role of LINE-1 hypomethylation in GC patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0507 GISTAR PILOT STUDY: GROUP DESCRIPTION AND PRELIMINARY RESULTS

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**Introduction:** Although recommended by international guidelines, limited data are available on the benefits and risks of a population-based *H. pylori* eradication ('search-and-treat') strategy from controlled clinical studies. Furthermore, the benefit of pepsinogen testing for risk stratification in Caucasian population has not been sufficiently studied.
**Aims & Methods:** GISTAR study is aimed at investigating the role of *H. pylori* eradication combined with non-invasive screening for precancerous lesions in the reduction of gastric cancer mortality in a predominantly Caucasian population in Northern and Eastern Europe. Study subject recruitment for the pilot study was conducted in Latvia.
**Results:** Altogether 3453 subjects (1826 men, 1627 women) in the age range 40–64 were recruited to the study between October, 2013 and December, 2015 in 4 different recruitment sites in Latvia: Cesis, Aluksne, Ludza and Saldus. *H. pylori* IgG seroprevalence (Biohit, Plc., Finland) was 68.3%. GastroPanel (Biohit, Plc., Finland) and Eiken (Eiken Chemical Co., Tokyo, Japan) pepsinogen tests were performed to non-invasively assess the gastric mucosal status. Over 1000 subjects have undergone upper endoscopy with an extensive biopsy work-up; all the biomarker-positive cases and a fraction of subjects with normal biomarkers were referred for endoscopy. Participants underwent a faecal immunochemical test as a benefit of study participation and all the subjects with a positive FIT were referred for colonoscopy. OC-Sensor (Eiken Chemical Co., Tokyo, Japan) FIT with cut-off 10 µg Hb/g faeces was used; the FIT positivity rate was 5.6%.
**Conclusion:** The pilot study has provided the background study population description for Latvia and will provide data on the prevalence of precancerous lesions and acceptance of participation in the interventions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0508 INFECTIOUS AGENTS AND COLORECTAL CANCER: ANY IMPLICATION OF HELICOBACTER PYLORI?

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**Introduction:** *Helicobacter pylori* (Hp) is the only bacterium with a potential carcinogen in humans, already established for gastric cancer. However, systemic effects have been proposed, including colorectal carcinogenesis. The involved mechanisms remain unknown, being gastrin a candidate trophic factor.

**Aims & Methods:** To determine the Hp role in the development of adenomatous polyps and colorectal cancer (CRC). **Methods:** Retrospective case-control study of a total of 1271 routine upper GI endoscopies, performed during 6 months. Selected 306 patients with additional evaluation of gastric Hp infection and 116 with at least one total colonoscopy. There were evaluated demographic variables, classic risk factors of CRC and conditions associated with hypergastrinemia (CAH).

**Results:** Hp gastric infection occurred in 37.9% (n = 44), being moderate to severe in 61.4% (n = 27). The development of adenomatous polyps/CRC occurred in 25.9% (n = 30), being more frequent in Hp-positive patients (45.5% vs13.9%; $p < 0.001$), with a 5-fold increased risk (OR 5.167; $p < 0.001$). The moderate to severe Hp infection was associated with an 11-fold increased risk (OR 11.188; $p < 0.001$). The CAH were present in 62.1% (n = 72). The development of adenomatous polyps/CRC was more frequent in CAH (22.4% vs 3.4%; $p = 0.001$), showing a 5-fold higher risk (OR 5.652; $p = 0.001$). After multivariate analysis, the only significant risk factors for the development of adenomatous polyps/CRC were moderate to severe Hp infection (OR 17.618; $p = 0.024$) and long-term proton pump inhibitors (PPI) use (OR 31.289; $p = 0.010$). There was no association with the classic risk factors of CRC.

**Conclusion:** Hp gastric infection was associated with a higher risk of adenomatous polyps/CRC development. Hp eradication (especially in moderate to severe infection) and the rational use of PPI may reduce colorectal cancer risk. In patients with indication for long-term PPI use, a more aggressive colorectal cancer surveillance could be considered. Further studies are needed to evaluate the real impact of Hp/gastrin in colorectal carcinogenesis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 10:30–17:00

**SMALL INTESTINAL I – POSTER EXHIBITION**

## P0509 DIFFUSION-WEIGHTED MAGNETIC RESONANCE FOR ASSESSING ILEAL CROHN'S DISEASE FIBROTIC STENOSIS: VALIDATION TROUGH COMPARISON WITH THE PATHOLOGIC SCORE OF SURGICAL SPECIMENS

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**Introduction:** Magnetic resonance enterography (MRE) is highly sensitive in revealing soft tissues inflammation. Diffusion-weighted imaging (DWI) can distinguish intestinal inflammation from a lower diffusion of water molecules giving rise to a reduced apparent diffusion coefficient. The magnetic resonance index of activity score (MaRIA) and Clermont score were recently developed for staging CD activity and bowel wall fibrosis. The aim of the study was to prospectively compare conventional MRI sequences, dynamic contrast enhanced (DCE) MRI and diffusion weighted imaging (DWI) with histopathology of surgical specimens in Crohn's disease to identifie degree of disease activity and fibrosis.

**Aims & Methods:** Thirty consecutive Crohn's disease patients undergoing surgical intestinal resection were selected. Every patient has been studied with MRE with T1, T2 and DWI sequences. Thirty patients with abdominal pain and without gross lesions undergoing MRE with the same protocol have been taken as controls. In Crohn's patients subgroup images have been analysed through quantitative (oedema, ulcers) and qualitative submucosal intensity signal (WSI), relative contrast enhancement (RCE), apparent diffusion coefficient (ADC) parameters. Tissue samples from surgical specimens have been analysed by a pathologist and have been calculated histopathological inflammatory and fibrosis scores. Correlation analysis and case-control studies were done by non-parametric tests and ROC curves has been realized to evaluate RM parameters' accuracy to predict fibrosis degree.

**Results:** None of traditional MRI parameters (%gain, wall thickness, relative contrast enhancement, ulcers or edema presence, MaRIA and Clermont agrees with the histological data of inflammation or with the fibrosis score (FS). ADC values instead inversely correlate with FS ($r = -0.517$: $p < 0.005$), amount of neutrophils ($r = -0.373$; $p = 0.045$), with the depth of neutrophilic penetration ($r = -0.428$; $p = 0.021$) and with acute inflammation score (AIS) ($r = -0.435$; $p = 0.019$). AIS and FS significantly correlate ($r = 0.431$, $p = 0.017$). An ADC value cutoff of 0.82 $10^{-3}$ $mm^2/s$ has high accuracy in predicting fibrosis with 75% sensitivity (95% CI 42.8–94.2) and 88.9% specificity (95% CI 65.2–98.3) with an AUC of 0.799. ADC can predict AIS value with an accuracy of 83.7% (95% CI 0.657–0.945) ($p < 0.0001$) for a cutoff value of 1 x $10^{-3}$ $mm^2/s$ (100% sensitivity and 63.2% specificity). A threshold value of 0.82 x $10^{-3}$ $mm^2/s$ ADC predicts the presence of neutrophils with a 83% accuracy (95% CI 0.65–0.94) ($p = 0.0001$), 100% sensitivity and 76% specificity. The depth of neutrophilic penetration is predicted with a 79% accuracy (95% CI 0.60–0.91) ($p = 0.0007$), 100% sensitivity and 60% specificity for a threshold value of 1 x $10^{-3}$ $mm^2/s$. ADC, RCE, MaRIA and Clermont were significantly different from CD patients to controls ($p = 0.019$ for RCE and $p < 0.0001$ for the others). The threshold value of 1.47 x $10^{-3}$ $mm^2/s$ is able to discriminate MC patients from healthy controls with 99.8% accuracy (95% CI 0.936–1.000), 96.7% specificity and 100% sensitivity.

**Conclusion:** MRE with DWI sequences provide important information in small bowel CD. ADC and MaRIA maps correlated with histopathological specimens and represent good predictors of both fibrosis and inflammation. In presence of a major fibrotic component ADC values tend to be low and it is possible to establish threshold values that can accurately identify patients who can be eligible for surgery.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0511 THE ROLE OF ZONULIN AND HAPTOGLOBIN GENOTYPE IN TYPE 1 DIABETES

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**Introduction:** Haptoglobin (HP) is an acute phase protein that in its mature form scavenges hemoglobin, averting oxidative activity following hemolysis. HP has a strong relationship with the development of inflammatory and autoimmune disorders and exists as HP1 and HP2 alleles resulting in 3 HP genotypes; HP 1–1; HP 2–1 and HP 2–2. The precursor of HP2 (pHP2) has been characterized as zonulin, a protein that causes physiological reversible disassembly of intestinal tight junctions (TJ) and altering permeability by regulating the paracellular pathway. It is hypothesized that zonulin is upregulated in individuals with type-1-diabetes (T1D) who carry the HP2 allele.

**Aims & Methods:** The aim is to determine if zonulin expression is increased in T1Ds who have a higher yield of HP 2 allele by comparing HP genotype with Zonulin expression. Serum and DNA from T1D and age, race and gender matched controls were selected from our biorepository. Samples were genotyped using specific primers to HP in exon 2 and 5 in HP1 and exon 2 and 7 in HP2. The quantification of zonulin in the serum samples was done by a semi-quantitative approach using a non-denaturing gel in native western blot followed by band densitometry of zonulin.

**Results:** A total of 322 individuals were genotyped for HP and quantified for zonulin. The distribution of HP genotypes is shown in Table 1. We observed a statistical difference between T1Ds and controls ($p < 0.05$) When segregating the HP genotype distribution by gender, we observed a significant difference in males ($P < 0.0002$), but not in females ($p = 0.5059$). In comparing pediatric T1D age of onset with HP genotype, we observed a correlation ($R^2 = 0.97$) trending toward a lower age of onset related to HP2 frequency. Furthermore, we saw a significant ($P < 0.0001$) zonulin increase in T1Ds with HP 2–2 compared with HP 2–1 and HP 1–1, which was not observed in controls ($P = 0.0912$). This observed increase in zonulin levels for the HP2 alleles was more represented in male T1Ds ($p = 0.0029$) compared with the female T1Ds ($p = 0.0103$). When we compared the T1Ds with controls for each respective HP genotype, no significant increase was observed in any group.

**Table 1**

| | T1Dm, n (%) | Controls, n (%) | P value |
|---|---|---|---|
| **Total** | 215 (66.8) | 107 (33.2) | 0.0465 |
| **HP 1–1** | 35 (16.3) | 25 (23.4) | |
| **HP 2–1** | 104 (48.3) | 46 (43.0) | |
| **HP 2–2** | 74 (34.4) | 36 (33.6) | |
| | **Female T1Dm, n (%)** | **Female Controls, n (%)** | **P value** |
| **Total** | 137 (63.7) | 74 (69.2) | 0.5095 |
| **HP 1–1** | 27 (19.7) | 17 (23.0) | |
| **HP 2–1** | 64 (46.7) | 35 (47.3) | |
| **HP 2–2** | 46 (33.6) | 22 (29.7) | |
| | **Male T1Dm, n (%)** | **Male Controls, n (%)** | **P value** |
| **Total** | 78 (36.3) | 33 (30.8) | 0.0002 |
| **HP 1–1** | 8 (10.3) | 8 (24.2) | |
| **HP 2–1** | 42 (53.8) | 11 (33.3) | |
| **HP 2–2** | 28 (35.9) | 14 (42.4) | |

**Conclusion:** There is a significant difference in distribution of HP genotypes when comparing controls with T1Ds presenting male subjects as highly statistically significant compared with females. Also, a lower age of onset in T1D pediatrics is related to a higher frequency of HP 2–2 compared with HP 2–1 and HP 1–1. Moreover, there is a significant correlation between T1D serum Zonulin levels compared with HP genotypes. This significance stronger in male T1Ds compared with female T1Ds.

**Disclosure of Interest:** A. Fasano: Stock holder Alba therapeutics.
All other authors have declared no conflicts of interest.

## P0512 WNT SIGNALING ACTIVATION IN THE GUT ANTI-INFLAMMATORY PROCESS DRIVEN BY THE HERBAL PREPARATION, STW5

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**Introduction:** In the last two decades, enormous progress has been made in the characterization of soluble and regulatory factors of gut functionality under physiological and inflamed conditions. Among signaling molecules, Wnt pathway components, including specific ligands (Wnts) and Frizzled (FZD) receptors, are reported to play a pivotal role in the homeostasis of intestine epithelium[1] and enteric neuronal surveillance from inflammatory stimuli.[2] The multi-component herbal preparation, STW5, has been effectively used clinically to treat functional gastrointestinal disorders.[3] Its mechanism of action seems to be multi-targeted, including anti-inflammatory and mucosal protective effects.[4, 5] In the present study, using in vitro models of gut inflammation, we investigated whether the activation of Wnt signaling is promoted by STW5 treatment.

**Aims & Methods:** Cells from enteric nervous system (ENSc) and epithelium (EPc) were isolated from the gut of adult Zebrafish (over 3 months of age) adapting known standardized procedures.[2, 6] After assessing in vitro-inflammatory conditions by stimulating for 24 h with 5 μg/mL lipopolysaccharide (LPS) or 0.5% dextran sodium sulfate (DSS), cell cultures were treated for 6 h and 24 h with 0.12 mg/mL lyophilized STW5. In parallel, resting cells and samples primed with only STW5 or LPS or DSS were used as controls. Thus, the analysis of Wnt signaling was performed evaluating the expression of IL1$\beta$, IL6, IL8, TNF$\alpha$, IL10 and Wnt3a by qPCR and the nuclear translocation of $\beta$-catenin and NF-$\kappa$B p50/p65 by Western blot.

**Results:** Isolation methods and in vitro culture conditions demonstrated to be effective to obtain functional ENS and EP cell cultures. Under inflammatory conditions, STW5 treatment downregulated mRNA expression of pro-inflammatory cytokines (IL1$\beta$, IL6, IL8 and TNF$\alpha$) and increased the gene expression of anti-inflammatory IL10 and Wnt3a. Interestingly, in resting and inflammatory conditions, STW5 showed to be functional to inhibit the nuclear translocation of p65, known to activate inflammatory response, while promoting a continuous nuclear shuttling of $\beta$-catenin, that, in contrast, is involved in anti-inflammatory process. Moreover, STW5 seemed to regulate NF-$\kappa$B transcriptional repression modulating the presence of NF-$\kappa$B p50 in the nucleus.

**Conclusion:** Our results provided the evidence that the activation of Wnt pathway is driven by STW5 treatment and leads to a negative regulation of NF-$\kappa$B inflammatory signaling in enteric epithelial and ENS compartments.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0513 PROTECTIVE EFFECT OF URSODEOXYCHOLIC ACID AGAINST CHEMOTHERAPY-INDUCED MUCOSITIS

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**Introduction:** Gastrointestinal mucositis is a serious side effect of chemotherapy. It increases the frequency of infection, risk of bleeding, and duration of hospitalization, consequently reducing subsequent chemotherapy doses. Ursodeoxycholic acid (UDCA), which is currently used in various liver diseases, exerts direct cytoprotective effects by stabilizing membranes, inhibiting apoptosis, and acting as an antioxidant. The protective effect of UDCA against chemotherapy-induced mucositis was assessed using an in vivo animal model.

**Aims & Methods:** Female Sprague-Dawley rats were randomly assigned to the following 5 groups: non-chemotherapy and vehicle; 5-fluorouracil (5-FU) and vehicle; 5-FU and 10 mg/kg/day UDCA; 5-FU and 100 mg/kg/day UDCA; and 5-FU and 500 mg/kg/day UDCA. 5-FU (400 mg/kg) or physiological saline (control) was administered by intraperitoneal injection. UDCA was orally administered 1 day before 5-FU injection for 6 days. One day after the final UDCA dose, rats were sacrificed, and the intestines were dissected for tissue sampling and laboratory analysis.

**Results:** UDCA promoted a higher body weight recovery, decreased villus destruction, and reduced inflammatory cytokines levels, at doses of 10 and 100 mg/kg/day. Villous fusion and destruction were pronounced in the 5-FU group compared with those observed in the UDCA-treated group or controls. The jejunal villous lengths were as follows: 212.8 ± 58.0 μm, 331.3 ± 18.0 μm, and 310.0 ± 112.6 μm, in the 5-FU and vehicle, 5-FU and 10 mg/kg UDCA ($p = 0.006$), and 5-FU and 100 mg/kg UDCA groups ($p = 0.046$), respectively. Real-time polymerase chain reaction (RT-PCR) showed that IL-6 and TNF-$\alpha$ levels decreased in the 10 mg/kg and 100 mg/kg UDCA co-administration groups. Further, myeloperoxidase activity decreased in the UDCA co-administration group.

**Conclusion:** UDCA significantly attenuated the reduction of the height of small intestinal villi and reduced inflammatory cytokine levels, thus highlighting the potential of UDCA as a preventive agent against chemotherapy-induced gastrointestinal mucositis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0514 EXPERIENCE WITH NALOXONE HYDROCHLORIDE FOR THE TREATMENT OF ACUTE COLONIC PSEUDOOBSTRUCTION

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**Introduction:** In acute colonic pseudoobstruction (Ogilve syndrome) there is dilation of the colon without mechanical obstruction, it may develop after surgery or with severe systemic illness. This condition is due to an acute imbalance of the normal extrinsic autonomic innervation of the bowel. Although it may resolve with conservative therapy, colonoscopic decompression is sometimes needed to prevent ischemia and perforation of the bowel. Studies suggest that neostigmine is an effective treatment. One report from our centre of Ryles tube administration of Naloxone, an opiod antagonist, which is a synthetic congener of oxymorphone, with good results. However there is no reported experience with Intravenous Injection Naloxone hydrochloride.

**Aims & Methods:** To study the efficacy of Injection Naloxone hydrochloride in patients acute colonic pseudoobstruction. We studied admitted patients fulfilling criteria of acute colonic pseudo-obstruction in the form of clinical abdominal distention and radiographic evidence of significant colonic dilation. Reversible and mechanical causes of abdominal distention ruled out. When there was no response to at least 24 hours of conservative treatment, we prospectively recruited patients to receive 0.4 mg Naloxone intravenous eight hourly. Clinical response was defined as evacuation of flatus or stool and a reduction in abdominal distention, abdominal circumference, and measurements of the colon diameter on radiographs. Patients who had no response to the initial dose were eligible to receive open-label Naloxone 24 hours later and subsequent doses 8 hrly for 24 hrs, if that fails then rescue Injection neostigmine and colonoscopic decompression were kept in treatment protocol.

**Results:** Prospectively total 25 patients were included in study since march 2015, eight patients were having pneumonia, septicaemia, three patients with chronic renal failure, septicaemia, five patient with cerebrovascular accident, two post spinal surgery, five with polytrauma due to road traffic accident, two post knee replacement. Twenty-one patients who received Naloxone had early colonic decompression in the form of passage of flatus, passage of motion, significant (more than 2 inch) decrease in abdominal girth, significant decrease in large bowel diameter on x-ray flat plate abdomen (equal or more than one cm), improvement in clinical parameters especially respiratory rate, oxygen saturation. In one patient colonoscopic decompression required, three had poor recovery. Injection Neostigmine was not used for any patient. Median time to response was 8 hours (range 3 to 28 hours). Side effects of Naloxone included mild tachycardia and rise in blood pressure in five patients, Irritability noted in 6 patients.

**Conclusion:** Our study suggests that Injection Naloxone is beneficial and safe in the treatment hospitalized patients with acute colonic pseudoobstruction. It obviates the need of Neostigmine which is associated with serious cardiac side effects and colonoscopic decompression which is not possible at every centre.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0515 ARE NUTRITIONAL BEHAVIOR, LIFESTYLE-FACTORS AND ANTIBIOTICS RISK FACTORS OF SMALL BOWEL BACTERIAL OVERGROWTH (SIBO)?

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**Introduction:** Established risk factors of small bowel bacterial overgrowth (SIBO) include anatomical (e.g. ileocecal resection) or physiologic (e.g. gastric hypoacidity) barrier dysfunctions as well as disturbed gut motility and mucosal immune deficiency. Mucosal immunity is suggested to be modulated by gut microbiota. Gut microbiota, in turn, are influenced by nutrition and antibiotics.

**Aims & Methods:** It was therefore the aim of our study to test associations between nutritional behavior and prior antibiotic treatments with the presence of SIBO. Consecutive patients, who presented with typical abdominal symptoms and performed a glucose H2-breath test for suspected SIBO, were asked to fill in questionnaires assessing nutritional behavior (including 'food frequency'), physical exercise, prior medical history including abdominal surgery and medication (including antibiotic therapies within the past two years). Associations between the questionnaire and breath-test results (SIBO confirmation: yes/no) were analyzed with t-test and Chi-square statistics.

**Results:** In the 191 participants (69% female, mean age 48), SIBO was confirmed in 26%. There were significant differences between SIBO-positive patients compared to patients with abdominal symptoms but normal glucose H2-breath test: SIBO patients were predominantly female (84%), had a lower BMI (21.4 vs. 23.9), and exercised less (53 vs. 104 min/week) (all $p < 0.05$). SIBO patients more often followed individual diets and consumed less sugary foods and drinks, less alcohol and less stodgy foods. Moreover, prior gastrointestinal surgery and frequent antibiotic treatment were significantly associated with SIBO (all $p < 0.05$).

**Conclusion:** In patients, who perform glucose H2-breath test because of abdominal symptoms, those with confirmed SIBO differ significantly from patients with normal breath test results, particularly regarding less physical exercise, altered nutritional behavior and more frequent prior antibiotic therapies. Whether these differences can be attributed to consequences (adaptation?) or causes (risk factors?) of SIBO should be addressed and clarified in future studies.

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All other authors have declared no conflicts of interest.

## P0516 A VALIDATION STUDY: INSERTION DEPTH MEASUREMENT IN SINGLE BALLOON ENTEROSCOPY IN PORCINE MODEL: CORRELATION WITH CAPSULE ENDOSCOPY

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**Introduction:** The exact length of small bowel (SB) explored during Balloon Enteroscopy and its correlation with Capsule Endoscopy (CE) is difficult to estimate. The insertion depth measurement using May's Method for Double Balloon Enteroscopy (DBE) was validated previously in animal model but there are no studies with single-balloon Enteroscopy (SBE).

**Aims & Methods:** 1. To validate the insertion distance with SBE by May's method in porcine a model. 2. To correlate the explored distance of SBE with CE time. Necropsy was used as gold standard. An oral SBE was performed during a maximum time of 120 minutes. Different marks, using colored clips, were done during the procedure every 30 minutes and, at the most distal insertion depth, an ink tattoo was injected. May's Method was used to assess the length of each insertion cycle (estimated 30–40 cm). 24 hours later, a CE was administered to the animal in order to localize the different SB marks. After euthanasia, the marks and distances were measured with a flexible ruler.

**Results:** 13 pigs were included. The average insertion depth estimated was 167.69+/-13.8 cm and 150.31+/-17.3 cm, with Maýs method and necropsy respectively; The Pearson correlation coefficient showed a good correlation between both measures ($r = 0.7$; $p = 0.004$). The average number of cycles performed during SBE was 8.29+/- 2.9. Regarding CE, average time to reach ink tattoo was 228.71+/-20.35 minutes, identifying 75% of marks previously done in SB.

**Conclusion:** 1. Maýs method is accurate to estimate depth insertion for SBE and might give approximate reference values in humans. 2. These data may help us estimate distances to reach a lesion detected by Capsule Endoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0517 DIAGNOSIS OF CELIAC DISEASE WITHOUT DUODENAL BIOPSY IN ADULTS WITH POSITIVE SEROLOGY TESTING

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**Introduction:** The latest ESPGHAN guidelines for the diagnosis of coeliac disease (CD) allow to avoid duodenal biopsy sampling in symptomatic children with genetic predisposition to CD who show immunoglobulin A anti-transglutaminase (IgA tTG) antibody titers >10 times the upper limit of normal range after confirmation of anti-endomysium antibodies (EMA) positivity. In adults, instead, small-bowel biopsy is still requested for the diagnosis of CD.

**Aims & Methods:** Our aim was to assess, in a large adult population with clinical suspicion of CD: 1) the PPV of specific serum antibodies (IgA EMA and IgA tTG), both alone and in combination, for histologically proven CD (Marsh-Oberhuber≥I); II) the cut-off value of IgA tTG correlated with the highest PPV for histologically proven CD in patients with positive EMA. We performed a retrospective analysis of a prospectively maintained database including all adult (age >16 year old) patients who underwent celiac serology testing between January 2004 and September 2015 at the "A. Gemelli" University Hospital. First, the electronic database of the Biochemistry Unit was searched to identify patients who resulted positive for IgA EMA and/or had IgA TTG >16 U/ml. Then, we searched the electronic database of the Histopathology Unit to determine how many of these patients underwent small bowel biopsy, and to retrieve related histology reports. Patients were excluded from the final analysis for the following reasons: pediatric age (<18 year-old); pregnancy; small bowel neoplasms; Whipple disease; Crohn's disease; duplicate testings; duodenal biopsy not performed/unavailability of histology report at our Center. The PPV of specific serum antibodies, alone and/or in combination, for histologically proven CD (Marsh-Oberhuber ≥1) was calculated. A ROC curve was generated to establish the cut-off value of IgA tTG correlated with the highest PPV for histologically proven CD in patients with positive IgA EMA. Accuracy parameters are reported as percentage [95% confidence interval].

**Results:** Between January 2004 and September 2015, a total of 57303 individuals underwent IgA EMA and/or IgA TTG; after removal of duplicate testings, we found 23531 patients who had undergone both testings; among them, 446 patients were positive for both EMA and tTG, 341 for EMA alone, and 436 patients for tTG alone, respectively. Histology reports were available for 178 patients. Of these patients, 38 (21%) had abnormal tTG alone, 19 (11%) had positive EMA alone, and 121 (68%) had positivity of both antibodies. Among the 19 subjects positive for EMA alone, 13 (68%) showed no alterations of duodenal mucosa, none showed Marsh-Oberhuber I or II lesions, and 6 (32%) showed Marsh-Oberhuber III lesions. The 38 subjects positive for tTG alone had no Marsh-Oberhuber lesions in 21 cases (55%), Marsh-Oberhuber I lesions in 1 case (3%), Marsh-Oberhuber II lesions in no cases, Marsh-Oberhuber III lesions in 16 cases (42%). Among the 121 patients with positivity of both antibodies, respectively 4 Marsh-Oberhuber I lesions (3%), 4 Marsh-Oberhuber II lesions (3%) and 113 Marsh-Oberhuber III lesions (95%) were identified. Positivity of both EMA and tTG in combination, positivity of EMA alone, and positivity of tTG alone achieved, respectively, a PPV for histologically proven CD (Marsh-Oberhuber ≥I) of 100%, 91%, and 86%. In patients with positive EMA, level of tTG ≥18 U/mL was identified as the best cut-off value for predicting Marsh-Oberhuber grade≥1, with a PPV of 100%, whereas level of tTG ≥34 U/mL was identified as the best cut-off value for predicting Marsh-Oberhuber grade≥2, with a PPV of 99.1%, and level of tTG ≥43 U/mL was identified as the best cut-off value for predicting Marsh-Oberhuber grade = 3, with a PPV of 97%.

**Conclusion:** Our preliminary findings suggest that CD can be diagnosed without the need of biopsy sampling in adult patients with positive EMA and tTG cut-off levels slightly higher than those used currently in clinical practice. Should our results be confirmed by further, larger studies, the diagnosis of CD based only on serology, without duodenal biopsy, may become a reasonable approach in a substantial subpopulation of the adult patients with clinical suspicion of CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0518 GENETIC VARIANTS ASSOCIATED WITH ANAEMIA IN ADULT COELIAC PATIENTS: THE ROLE OF TMPRSS6 AND HFE

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**Introduction:** Coeliac disease (CD) is a chronic, immune-mediated disease occurring in genetically predisposed individuals who assume gluten. Iron deficiency anaemia (IDA) is very common in CD and has been reported in up to 46% of cases of subclinical CD. Even though the link between malabsorption and anaemia is well known, the role of genetic factors remain unexplored.
**Aims & Methods:** We speculated that common SNPs of iron metabolism genes would be associated with anaemia of CD patients. From October 2011 to July 2015 we prospectively assessed the frequency of TMPRSS6 variant rs855791 and HFE variants rs1800562 and rs1799945 in both anemic and non-anemic CD patients at time of CD diagnosis. We also estimated the association of these variants with some hematological and iron parameters (Hb, MCV, serum iron and serum ferritin). Statistical analysis was performed by using T-student and X-square test when indicated; all differences were considered significant when $p < 0.05$.
**Results:** Finally, 491 patients were enrolled: 266 with IDA (mean age 31.2; females 88%), 225 with non-IDA (mean age 32.4; females 65%). TMPRSS6 variant rs855791 and HFE variant rs1799945 were found higher in non-IDA than IDA CD patients (52.2% vs 47% and 27% vs 24.5%, respectively), although not statistically significance ($p = 0.1$). Conversely, HFE variant rs1800562 was found to be significantly higher in IDA than non-IDA CD patients (3.4% vs. 0.8%, $p = 0.03$). Furthermore, CD subjects with TMPRSS6 variant rs855791 showed higher Hb and serum ferritin and lower MCV and serum iron level compared to CD subject with TMPRSS6 WT variant. IDA subjects with HFE variant rs1800562 showed increased serum iron and ferritin values in comparison with CD subject carrying the wild type variant.
**Conclusion:** In CD patients, HFE variant rs1800562 appeared to be more frequent in IDA than in non-IDA and it associated with higher iron status, so conferring a protective role regarding IDA in CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0519 FODMAPS FREE DIET: AN EFFECTIVE SOLUTION FOR SYMPTOMATIC COELIAC PATIENTS ON GLUTEN-FREE DIET

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**Introduction:** Recent studies have shown high efficacy of a FODMAPs free diet (FFD) in patients suffering from non-coeliac wheat sensitive (NCWS) and irritable bowel syndrome (IBS), but data on this kind of dietary approach in coeliac disease (CD) are still scarce.
**Aims & Methods:** Aim: to establish the efficacy of FFD in symptomatic CD patients despite being on gluten-free diet (GFD), also comparing this outcome with that of subjects affected by IBS.
**Methods:** From January 2016 to September 2016 we carried out an observational prospective study including all consecutive adult CD patients (Group A) who were symptomatic (abdominal pain, diarrhoea, bloating, constipation) despite performing a strict GFD. Also, we enrolled all consecutive adult IBS patients (Group B) referred to our general Ambulatory. We administered a personalized FFD and 2 questionnaires (IBS-SSS with a pain score from 0-minimum to 3-maximum, and SF-36 with 8 different domains) at the time of the first visit (T0), 1 month after (T1) and at 3 months (T3) from the beginning of FFD. Statistical analysis included ANOVA test with and without covariates adjustment. All results were considered significant with a $p < 0.05$.
**Results:** Finally, 66 patients were enrolled (Group A: 23 vs Group B: 43). All CD patients were on GFD from at least 1 year and showed negative EMA and anti-transglutamineases. No differences were noted in terms of age and gender (P = NS). When analyzing the IBS-SSS results, the symptomatic score dropped in both Groups after starting FFD (Group A: 2.04 at T0, 1.26 at T1 and 1.09 at T3 ($P < 0.01$); Group B: 2.35 at T0, 1.42 at T1 and 1.07 at T3 ($P < 0.01$)). However, no statistically significant differences were noted between the two Groups (P = NS). When analyzing the results from SF-36, no differences were noted between the two Groups, even though both CD and IBS population significantly improved their own status with the regards of the 8 domains of SF-36, both at T1 ($P < 0.01$) and at T3 ($P < 0.01$).
**Conclusion:** FFD leads to a significant improvement of gastrointestinal symptoms in CD patients who were persistently symptomatic despite GFD. GFD in association with FFD should be considered a first-line therapy CD this population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0520 VALUE OF FOLLOW-UP CONTROL BIOPSY AND SIGNIFICANCE OF INCOMPLETE MUCOSAL RECOVERY CELIAC DISEASE

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**Introduction:** A repeat biopsy is recommended in celiac patients on a gluten-free diet, but for variable reasons it is often omitted. We sought factors associated with lacking endoscopic follow-up and significance of this to the long-term treatment results. Furthermore, predictors and significance of histological recovery was investigated in re-biopsied patients.
**Aims & Methods:** 760 previously diagnosed patients participated to a nationwide follow-up study. A wide selection of medical data at celiac disease diagnosis and at present were gathered through interviews and via patient records and blood samples were drawn for serology. Current symptoms and quality of life were assessed by validated questionnaires. Next, all study data was compared between participants with and without a repeat biopsy, and between those with and without histological recovery in re-biopsy.
**Results:** Altogether 68% had undergone a repeat biopsy. Factors predicting this were presence of malabsorption (46% vs 33%, $p < 0.001$) and severe symptoms (24% vs 16%, $P = 0.05$) at diagnosis and concomitant gastrointestinal (40% vs 32%, $P = 0.049$) or locomotor (35% vs 27%, $p = 0.023$) disease, whereas it was less likely in subjects diagnosed in private care (11% vs 23%, $P < 0.001$) or by screening (10% vs 16%, $P = 0.010$). The groups did not differ in the current self-estimated symptoms and dietary adherence, but non-biopsied subjects were less confident of their diet (89% vs 94%, $P = 0.002$) and were more often endomysial antibody-positive (14% vs 9%, $P = 0.012$). However, they reported better SF-36 physical functioning (0.043) and pain (0.013) scores and GSRS indigestion (0.046) and total (0.052) score. Incomplete mucosal recovery in re-biopsied patients ($n = 476$) was predicted by more advanced histological ($P < 0.001$) and serological ($P = 0.001$) disease at diagnosis and presence of concomitant respiratory ($P = 0.031$) and dermatological (0.043) diseases, while the groups did not differ in the other co-morbidities and current adherence or capability to manage gluten-free diet, seropositivity, self-estimated symptoms and questionnaire scores.
**Conclusion:** Patients with more severe disease at diagnosis were more prone to undergo repeat biopsy and also not reaching full mucosal recovery if re-biopsied. However, neither lack of repeat biopsy nor incomplete histological recovery were associated with poorer long-term dietary adherence or clinical response.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0521 MARKERS OF INNATE IMMUNITY AND GUT PERMEABILITY IN COELIAC DISEASE PATIENTS WITH PERSISTENT SYMPTOMS ON A GLUTEN-FREE DIET

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**Introduction:** For unexplained reasons a part of the coeliac disease patients suffer from persistent symptoms despite a strict gluten-free diet (GFD) and lack of co-morbidities (1). We investigated the role of dietary factors, innate immunity, epithelial stress and integrity in this setting by comparing long-term treated coeliac disease patients with and without persistent symptoms.
**Aims & Methods:** Altogether 22 asymptomatic and 25 symptomatic coeliac disease patients on a GFD were enrolled. They completed a four-day food diary and clinical, serological and histological data were analyzed. Further, density of CD3+ and $\gamma\delta$+ intraepithelial lymphocytes (IELs), CD25+ and FOXP3 regulatory T cells and CD117+ mast cells, and the expression of Claudin-3 tight junction protein, heat shock protein 60 (HSP60) and interleukin 15 (IL15) were evaluated from small-bowel mucosal biopsies.
**Results:** All subjects were on a strict GFD and had negative coeliac autoantibodies and recovered mucosal villi. The groups did not differ in the use of wheat starch and purified oats, but asymptomatic patients had higher mean fiber intake than those with symptoms (20.2 vs. 15.2 g/day, $p = 0.028$), although there was wide individual variation. Asymptomatic subjects had higher density of CD3+ IELs than those with symptoms (59.3 vs. 45.0 cell/mm, $p = 0.045$) and there was

similar but non-significant trend in γδ+ IELs (17.9 vs. 13.5, p = 0.149). There were no differences between the groups in the intensity of CD25+, FOXP3, CD117+ and IL15 stainings, but some patients with persistent symptoms had weaker Claudin-3 staining and stronger HSP60 staining.
**Conclusion:** Our results indicate that some coeliac disease patients with persistent symptoms could benefit from a diet rich in fiber. Most of the study markers were not associated with the presence of symptoms, but there might be a subgroup of symptomatic patients exhibiting increased epithelial stress and compromised integrity. Somewhat surprisingly, asymptomatic patients had even higher density of mucosal IELs, suggesting that there is no direct association between these cells and persistent symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0522 THE LIVER IN CELIAC DISEASE: A MOROCCAN SINGLE-CENTER EXPERIENCE

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**Introduction:** Celiac disease is an autoimmune enteropathy that may be associated with various extra-intestinal manifestations. Liver disease is one of the most frequent.
**Aims & Methods:** Clinical data of 91 patients with celiac disease associated with abnormal liver tests were retrospectively studied and analyzed, during a period of 20 years, from January 1995 to December 2015. The aim of this study is to show the different forms of liver diseases that can be associated to celiac disease ant the impact of a gluten free diet in the evolution of those liver abnormalities.
**Results:** The mean age of the patients was 34 years and they were aged between 13.5 and 61 years old. There was a feminine predominance with sex ratio women/men of 4. The discovery of the liver disease was concomitant with the diagnosis of celiac disease in 86.8% of cases, and found first, before the diagnosis of celiac disease in 13.2% of cases. The most frequent liver disase found was represented by hepatic steatosis, nonalcoholic steatohepatitis, cryptogenic hypertransaminasemia and cryptogenic cirrhosis. Celiac disease was associated with autoimmune hepatitis in 6 cases, primary biliary cirrhosis in 2 cases, idiopathic portal hypertension in 2 cases, portal vein thrombosis by hymerhomocysteneimia or prothrombotic proteins deficiency in 5 cases, sarcoidosis in 2 case and a tuberculoid granulomatous hepatitis in 3 cases and hepatocellular carcinoma in one case. All our patients taked a gluten-free diet and deficiency supplementation, The follow up was weekly to evaluate the evolution of the disease. Celiac disease evolution was favorable in 90.1% and the evolution of the liver diseases was marked by the normalization of the liver function tests in the cryptogenic hypertransaminasemia after the start of gluten diet in 100% of cases. The normalization of biologically and ultrasound features in hepatic steatosis, and the stabilization of the cryptogenic cirrhosis in 71.42% of cases. We noted the normalization of the liver tests in the autoimmune hepatitis and the primary biliary cirrhosis after specific treatment of those 2 diseases.
**Conclusion:** Liver disease is frequent in celiac disease. Therefore celiac disease should be systematically looked for in any patient with unexplained chronic liver tests abnormalities, even in the absence of any gastrointestinal symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0523 SERUM 25-HYDROXYCHOLECALCIFEROL LEVELS AT CELIAC DISEASE PRESENTATION PREDICT BONE MINERAL DENSITY RECOVERY AFTER GLUTEN EXSCLUSION

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**Introduction:** Celiac disease (CD) patients at presentation variably show reduced bone mineral density (BMD) and altered bone-related serology, including serum 25-hydroxycholecalciferol (25[OH]-VitD). Gluten-free diet (GFD) has been shown to promote repair in children and to a smaller extent in adults[1]. However, complete bone mineral recovery is uncertain and predictive markers are lacking.
**Aims & Methods:** We aimed to evaluate the prevalence of reduced BMD (expressed as Z-score) at CD presentation, assess recovery under GFD and identify potential predictors of bone tissue recovery.
We included consecutive adult IgA anti-tTG positive, biopsy proven CD patients. BMD Z-scores were obtained by Dual Energy X-Ray Absorptiometry of the left femoral neck at diagnosis and during follow-up. GFD compliance at inclusion was assessed serologically.
**Results:** We evaluated 161 celiac adults (mean age = 39.2 years, F/M = 5:1) at diagnosis and after adequate GFD (mean duration 7.4 ± 6.8 years). Histology was graded according to the Corazza-Villanacci classification (Grade A = 10.6%, B = 50.9%, C = 38.5%). Mean IgA anti-tTG levels at onset were 73.3 ± 35.4 U/dl (mean±SD), while at inclusion 4.4 ± 2.3 U/dl. BMD Z-scores were lower at diagnosis (−1.6 ± 1.09 vs −0.9 ± 0.89, $p < 0.001$), showing no correlation with sex but moderately with age ($r = -0.221$, $p = 0.04$). Prevalence of normal vs low BMD (< −1.0 DS) at onset and inclusion was 18.6% vs 81.4%, and 27% vs 73%, respectively. Prevalence of severely reduced BMD (< −2.5 DS) at diagnosis was 14.8% vs 1.2% after GFD. Mean 25[OH]-VitD levels at inclusion were 17.07 ± 6.44 vs 26.71 ± 6.74 ng/dl after GFD ($p < 0.001$). Prevalence of deficit/insufficiency at diagnosis were 20.8%/66.7% vs 4.9%/62.3% after GFD, respectively. BMD at diagnosis did not correlate with GFD outcome ($r = -0.41$, $p = 0.581$). 25[OH]-VitD levels showed no correlation to BMD at onset. However, they correlated with BMD outcome ($r = 0.419$, $p = 0.041$). In particular, 25[OH]-VitD serum titers over a cut-off level of 20 ng/dl were significantly associated to higher BMD values after GFD (−0.24 ± 0.85 vs −1.12 ± 0.94, $p = 0.033$). Overall, mean GFD duration necessary to achieve a statistically significant BMD increase from diagnosis was 48 months (−1.46 ± 1.05 vs −1.04 ± 0.85, $p = 0.029$).
**Conclusion:** Reduced BMD is common in adult celiacs at diagnosis and generally responds slowly to GFD, potentially taking up to 4 years before significantly improving. Initial severity of BMD loss does not seem to impair recovery. Serum 25[OH]-VitD titers at onset positively correlate with outcome BMD; a cut-off of 20 ng/dl in our sample predicted an almost complete BMD recovery. Further studies are needed to confirm this potential predictor of outcome under GFD and its use as a marker for early treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0524 CLINICAL OUTCOME OF PATIENTS WITH RAISED INTRAEPITHELIAL LYMPHOCYTES (IELS) WITH NORMAL VILLOUS ARCHITECTURE ON DUODENAL BIOPSY

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**Introduction:** Intestinal intraepithelial lymphocytes (IELs) belong to a unique T-cell population interspersed between epithelial cells of the small intestine. IELs are the first line of host immune defense and are involved in intestinal immune surveillance with levels increasing in response to antigenic stimulation. (1) The normal IEL count has been recommended to be less than 25 IELs per 100 enterocytes based on duodenal biopsies being obtained endoscopically with histology performed on sections cut at 3–4 μm. (2, 3). The finding of a raised intraepithelial lymphocytes (IEL) count with normal villous architecture is of sufficient clinical importance to be reported in routine duodenal biopsies and remains a management challenge. Raised IELs with preserved villi are a feature of latent coeliac disease (CD). However they are also seen in a number of other conditions. Follow-up data from clinical practice may help identify at risk patients.
**Aims & Methods:** To determine the long-term clinical relevance of isolated increased IELs on random duodenal biopsy in an Irish cohort, with reference to subsequent coeliac disease development. A single tertiary center retrospective observational cohort study was undertaken. Patients from 2012 to 2014, > 18 years with at least one biopsy from the second part of duodenum with increased IELs; defined as > 25IELS/100 enterocytes, with preserved villous architecture were identified from our histopathology database. Patients were excluded if they had a history of Coeliac Disease (CD). Clinical and demographic data were recorded following a chart review. CD was diagnosed by the attending Physician based on the Physician Global Assessment. Data was compared between groups using a student t-test and odds ratios were calculated as appropriate. Statistical significance was set a priori at $p < 0.05$.
**Results:** Over 24 months 6,244 patients had duodenal biopsies and 114(1.8%) had isolated increased IELs. The mean age was 50 years (19–91) and 34(30%) were male. Follow-up was available in 75(65%), with a mean duration of 22 months. CD was subsequently diagnosed in 32% (n = 24). CD was associated with female gender 22/24 v 39/51, OR 7.5, $p < 0.05$, 95%CI 0.74–0.01 and older age 55 v 41 years, $p < 0.04$, 95%CI 26.8 - 0.28, In addition, a higher IEL count was predictive of CD with an IEL of > 40 in 11/24 (46%) with CD v 12/51 (24%) without CD, $p = 0.0006$, OR 5.6, 95% CI −0.54 to –0.15. Overall raised IEL's could be attributed to CD in 24 (32%), associated conditions / medications in 21(28%), *H.Pylori* infection in 14 (19%) and no cause was found in 24 (32%).

Clinical features and subsequent coeliac disease development

| Parameter | CoeliacN = 24 | Non-Coeliac N = 51 | p-value | OR |
|---|---|---|---|---|
| Age | 55 | 41 | <0.05 | N/A |
| Female | 22 | 39 | <0.05 | 7.5 |
| Positive TTG | 14 | 0 | <0.001 | 139 |
| H.Pylori infection | 10 | 14 | 0.36 | N/A |
| Associated medical conditions | 9 | 12 | 0.12 | N/A |
| IEL>40 | 11 | 12 | <0.001 | 5.6 |

**Conclusion:** Raised IELs are a frequent non-specific but important finding. In our cohort a third of patients subsequently developed CD. Of import a negative baseline TTG does not exclude CD development, NPV 85%. Close follow up of older female patients and those with IELs > 40 is supported by this data.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0525 COMPARING DIETITIAN-LED GROUP CLINICS TO INDIVIDUAL APPOINTMENTS FOR NEWLY DIAGNOSED PATIENTS WITH COELIAC DISEASE (CD)


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**Introduction:** Newly diagnosed CD patients should have a nutritional assessment and gluten-free diet (GFD) education by registered dietitians, in accordance with guidelines. Achieving these standards is problematic due to increased CD diagnosis and limited trained dietitians available to deliver these services. Locally, we have shown that patients often wait four to six weeks for a dietetic consultation following CD diagnosis, with patient feedback suggesting this is unacceptably long. This study aimed to address this concern by comparing whether dietetic consultations provided in group clinics was non-inferior to an individual appointment for newly diagnosed CD patients.
**Aims & Methods:** Between January 2015 and December 2015 newly diagnosed CD patients were seen either by a dietitian in a group clinic or in an individual appointment as part of a local service evaluation project. Group clinics were defined as having a minimum of 6 individuals, and covered the same topics as individual appointments (education on gluten-free diets, prescriptions, travelling and information on Coeliac UK). All patients had nutritional assessments at baseline and bloods performed in accordance with BSG guidelines. These were reassessed at 3-month follow-up appointments, alongside evaluation forms for clinics and assessment of GFD adherence using the Biagi score (A validated 5 point adherence score (0–4), with the highest score indicating strict GFD adherence). Comparisons between groups were made using a student t-test, with a p-value $< 0.05$ considered significant.
**Results:** 56 new CD patients were initially referred for a dietetic consultation. Eight patients (14%) did not attend first appointments and 8 failed to attend follow-up. Of the remaining 40 patients (25 F:15 M, mean age 48 years), 30 were seen in group clinics and 10 had individual appointments. There was no statistically significant difference in baseline BMI ($p = 0.57$), age ($p = 0.10$) or tissue transglutaminase antibody levels ($p = 0.54$) between group patients and individual clinic patients. At follow-up mean GFD adherence scores were similar in both groups (3.3 vs 3.1, $p = 0.51$), with paired t-tests showing significant reduction in both groups in serological markers and haematinics ($p < 0.001$). Evaluation forms supported the merits of group clinics, with 97% (29/30) of patients stating that group clinics met expectations, enhanced understanding and that they would recommend to other patients.
**Conclusion:** This study demonstrates how group dietetic clinics for newly diagnosed patients may be a resource saving intervention, which derives no detriment to patient education and GFD adherence. Findings from this work provide proof of concept for undertaking a future randomised controlled trial in this area, including health economic analysis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.



### P0526 CIRCULATING MICRORNA ASSOCIATED WITH VISCERAL OBESITY: A POSSIBLE BIOMARKER OF DIGESTIVE CANCERS


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**Introduction:** Visceral obesity is a key risk factor for the development of several digestive malignant diseases, such as esophageal adenocarcinoma, colorectal adenocarcinoma, and pancreatic ductal adenocarcinoma. Recently, circulating microRNAs (miRNAs) have been proposed as noninvasive biomarkers of diseases and potential therapeutic targets.
**Aims & Methods:** The aim of this study is to examine whether the level of visceral obesity-associated circulating miRNAs could be a novel biomarker for the presence of digestive cancers. We obtained serum samples from healthy individuals who received thorough medical examinations including the measurement of visceral fat area by abdominal computed tomography at Keio University Hospital between February 2015 and June 2015 as a training set. We also obtained serum samples from the healthy volunteers at Yokohama Minoru Clinic in 2015 as a validation set. We comprehensively evaluated serum miRNA expression profiles using microarray analysis. The training set was used to identify miRNAs which were associated with both the levels of visceral fat area (VFA) and body mass index (BMI). Subsequently, BMI-associated miRNAs were refined using the validation set. Finally, the associations between the presence of digestive cancers and the expression levels of the identified miRNAs were evaluated using a published dataset in the Gene Expression Omnibus database (GSE59856).
**Results:** A total of 83 and 1991 individuals were enrolled in the training set and the validation set, respectively. Levels of 9 miRNAs were positively correlated with both the levels of VFA and BMI in the training set. In the validation set, 2 of 9 miRNAs correlated with BMI were identified. Levels of both 2 miRNAs were also positively correlated with levels of HbA1c. Regarding one of the 2 miRNAs, the expression levels were significantly associated with the presence of pancreatic ductal adenocarcinoma (area under the ROC curve [AUC], 0.75; 95% confidence interval [CI], 0.68 to 0.81), hepatocellular carcinoma (AUC, 0.72; 95% CI, 0.64 to 0.79), colorectal adenocarcinoma (AUC, 0.69; 95% CI, 0.61 to 0.77), and biliary tract cancer (AUC, 0.67; 95% CI, 0.60 to 0.74), and were marginally associated with the presence of esophageal squamous cell carcinoma (AUC, 0.66; 95% CI, 0.58 to 0.74) and gastric adenocarcinoma (AUC, 0.65; 95% CI, 0.57 to 0.73).
**Conclusion:** We identified circulating miRNAs which were associated with visceral fat in large cohorts. Levels of a given miRNA were associated with the presence of pancreatic cancer, hepatic cancer, and colorectal cancer. This miRNA could be a biomarker of obesity-related digestive cancers, and be a target for the prevention of them.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0527 INDIVIDUALIZED RESPONSES TO LIFESTYLE INTERVENTIONS CAN BE PREDICTED BY GUT MICROBIOTA


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**Introduction:** Recent evidence suggests that the gut microbiota has a role in the pathophysiology of obesity by influencing host energy metabolism and adiposity. However, there is still limited evidence if pre-intervention characteristics of the gut microbiome will predict response to lifestyle interventions aimed at achieving weight loss.
**Aims & Methods:** The primary aim of this study is to determine if baseline differences in the gut microbiota are predictive of weight loss after a lifestyle intervention program in overweight and obese individuals. 27 obese and overweight individuals were recruited to participate in a lifestyle intervention program that included cognitive/behavioral therapy, a nutritional intervention, and a physical activity intervention. The nutritional intervention involved a volumetric approach that included unlimited fruits and vegetables and lower energy density foods with greater nutrient density. The physical activity intervention involved walking at least 10,000 steps per day. Subjects were followed every week during the first 3 months, every 2 weeks during the next month, and monthly thereafter. Height and weight measurements were obtained at baseline, 3 months, and 6 months after initiation of the intervention program. Percent of baseline weight loss was also calculated and a 5% weight loss was defined as success. Fecal stool samples were collected at baseline, 3 months, and 6 months. The V4 variable region of bacterial 16 S rRNA was amplified from stool DNA and sequenced with the MiSeq Illumina platform. Data analysis was done using Quantitative Insights into Microbial Ecology (QIIME 1.9.1) pipeline. The linear discriminant analysis (LDA) effect size (LEfSe) method was performed to identify significantly discriminative bacteria between subjects who failed or succeeded in achieving weight loss. An alpha of 0.05 and LDA threshold of >2.0 were used.
**Results:** 3 overweight and 24 obese individuals were included in the analysis. Mean age was 54 years (95% CI: 50.7, 57.1) and 78% were female. Average weight at baseline was 96.0 kg (95% CI: 90.4, 101.4) and average BMI at baseline was 34.1 $kg/m^2$ (95% CI: 32.8, 35.4). At 3 months, subjects achieved a mean

weight loss of 3.71 kg (95% CI: 2.31, 5.11) and a mean reduction in BMI of 0.80 (95% CI: 0.38, 1.57), with 9 subjects (33%) achieving at least a 5% weight loss. 8 of these subjects (89%) maintained a 5% weight loss at 6 months. Gut microbiota analysis showed no significant changes in alpha diversity or beta diversity after 3 months or 6 months. Subjects who achieved a 5% weight loss had baseline microbiota significantly enriched with Phascolarctobacterium, Corynebacterium, Cerasicoccaceae family, Oxalobacter, and Turicibacteraceae family bacteria. Those who failed to achieve a 5% weight loss had microbiota enriched with Veillonella and Pasteurellaceae family bacteria. Interestingly, both Phascolarctobacterium and Veillonella are members of the Veillonellaceae family and were the most discriminant taxa for each group, respectively, suggesting a potential nutrient niche competition in different states.
**Conclusion:** In this study, we identified discriminant gut microbiota that predict successful weight loss in participants of a comprehensive lifestyle intervention program. These pilot data support future developments of microbiota-based individualized strategies for weight loss.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0528 ENDOGASTRORIO CLINIC EXPERIENCE IN THE TREATMENT OF EXCESS WEIGHT USING THE SPATZ3 BALLOON

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**Introduction:** The intragastric balloon (IGB) is established as a safe and effective option to treat overweight/obesity, however, the balloons available untill now were not adjustable, and the maximum permanence was six months. Recently, the adjustable twelve months stay IGB Spatz3® has been approved for use in Brazil, and EndogastroRio clinic pioneered the use of this device in this country.
**Objective:** To evaluate the results and complications during the initial thirteen months of using the IGB Spatz3® in EndogastroRio clinic.
**Methods:** 155 patients were analyzed. The IGB Spatz3® was filled with a standard volume of 600 ml. The patients presented a minimum body mass index (BMI) 27 kg/m$^2$. Data were analyzed using descriptive statistic and the Student t test.
**Results:** Of 155 patients, 13 were excluded due to early IGB removal: three by intolerance and rejection of setting down the volume, one by a gastric ulcer due to non-use of proton pump inhibitor, eight for withdrawal of treatment non correlated with the adaption period sintoms, and one due to baloon ruption nine months after the implant and the not desire to replace it. The complications were: 5 (3.22%) gastric ulcers (4 observed only in the removal of the balloon, flat and asymptomatic). 1 (0.81%) case of gas production inside the balloon. Six balloon leakages: three balloons ruption due to cândida colonization, and three early leakages due to a deffective valve. One case of Mallory-Weiss syndrome. Of all patients, 9 underwent volume reduction of the balloon due to intolerance (mean 180 ml): Seven at the beginning of the treatment, and two after the upward setting, with clinical improvement and maintenance in treatment. Of the 142 remaining patients, 45 patients (33 female) have already completed the treatment and removed the balloon after a minimum period of nine months of balloon use. The final BMI ($31.88 \pm 6.38$ kg/m$^2$) was significatively lower than the initial BMI ($38.68 \pm 5.47$ kg/m2) ($p < 0.0001$). The average weight loss in kilograms was $18.84 \pm 11.21$. %TBWL was $17.65 \pm 10.02$, %EWL of $56.64 \pm 36.49$. 30 patients did the upward adjustment of the balloon during the treatment (mean 284.67 ml). There was no difference between the two groups in relation to kg weight loss ($p = 0.4144$), %TBWL ($p = 0.2754$) and %EWL ($p = 0.1739$)
**Conclusion:** Treatment with IGB Spatz3 shows to be safe (despite a higher incidence of ulcers, they are mostly asymptomatic), effective, without early removals in intolerant patients that were submitted to the down setting balloon volume.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0529 ASPIREASSIST AS A TOOL TO TREAT OBESITY: 1, 2, AND 3 YEAR RESULTS TO DATE IN 100-SUBJECT ONGOING MULTI-CENTER POST-MARKET STUDY

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**Introduction:** The AspireAssist System (Aspire Bariatrics, Inc. King of Prussia, PA) is a device to help people with obesity lose weight, consisting an a customized percutaneous endoscopic gastrostomy (PEG) tube and an external device to facilitate removal of approximately 30% of ingested calories consumed in a meal, in conjunction with lifestyle (diet and exercise) counselling.
**Aims & Methods:** A total of 100 subjects were enrolled from June 2012 to December 2015 as part of a post-market study involving 6 centers: University of Ostrava, in Ostrava, Czech Republic, Blekinge County Hospital in Karlskrona, Sweden; Teknon in Barcelona, Spain; L'Ospedale San Raffaele in Milan, Italy; a private clinic in Kufstein, Austria; and Herzog-Karl Klinik in Stuggart, Germany. Mean baseline BMI of the 100 subjects was $44.9 + 8.3$ kg/m$^2$.
**Results:** As of January 5, 2016, 80, 25, and 15 patients have reached 1, 2, and 3 years of therapy, respectively. Of the 100 subjects that enrolled, 17 patients have had their gastrostomy tube removed and are no longer part of the study: 6 before 1 year, 8 between 1 and 2 years, and 3 between 2 and 3 years. Mean (±SD) %EWL for the patients that completed 1, 2, and 3 years of therapy was 46.5% (24.3%), 55.1% (25.7%), and 56.2% (29.8%), while mean (±SD) %TBL was 18.8%(8.4%), 23.5%(8.8%), and 21.0%(10.2%), respectively. The most frequently reported adverse events were abdominal pain and discomfort in the perioperative period and skin irritation around the stoma in the postoperative period. Serious adverse events were reported in 4% of participants. There was no evidence to date of the development of any metabolic abnormality, nor any abnormal eating behaviors in patients in this study.
**Conclusion:** The AspireAssist System provides an effective weight-loss therapy, with few and minimal complications, for people with Class II and Class III obesity.
**Disclosure of Interest:** E. Machytka: Aspire Bariatrics – research and travel grant, consulting
All other authors have declared no conflicts of interest.

## P0530 COMBINATION OF OMEGA-3 FATTY ACIDS WITH ALIVE PROBIOTIC ARE SUPERIOR THAN PROBIOTIC ALONE FOR NAFLD PREVENTION

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**Introduction:** Today probiotics have been suggested as a treatment for the prevention of NAFLD. Omega-3 fatty acid treatment may have beneficial effects in regulating hepatic lipid metabolism, adipose tissue function, and inflammation.
**Aims & Methods:** The present study was designed to determine whether probiotics plus omega-3 as adjunct are superior to probiotic alone on the monosodium glutamate (MSG) induced NAFLD model in rats.
**Methods**. We included 60 rats divided into 4 groups 15 animals in each. Rats of group I were intact. Newborns rats of groups II-IV were injected with MSG (4.0 mg/g body weight) subcutaneously at postnatal days 2, 4, 6, 8 and 10. The III (Symbiter) group received 2.5 ml/kg of multiprobiotic "Symbiter" containing concentrated biomass of 14 probiotic bacteria genera Bifidobacterium, Lactobacillus, Lactococcus, Propionibacterium. The IV (Symbiter-Omega) groups received "Symbiter Omega" combination of probiotic biomass supplemented with flax and wheat germ oil (250 mg of each, concentration of omega-3 fatty acids 1–5%). Administration was started at 4 weeks after birth and continued intermittently two-week course in 2 weeks intervals. To assess morphological changes in liver we used NAS (NAFLD activity score). Lipid extraction from liver was performed according to Folch. The content of proinflammatory cytokines (IL)-1$\beta$, IL-12Bp40, INF-$\gamma$) and anti-inflammatory cytokines (IL-4, IL-10, TGF-$\beta$) were measured by ELISA.
**Results:** In both interventional groups reduction of total NAS score as compared to MSG-obesity was observed. Supplementation of alive probiotics mixture with omega-3 leads to more pronounced reduction for steatosis degree ($0.73 \pm 0.11$ vs $0.93 \pm 0.22$, $p = 0.199$) which accompanied with significant decreasing of triglyceride $5.1 \pm 0.25$ vs $6.26 \pm 0.23$, $p < 0.05$) accumulation in liver as compared to probiotic alone. For both intervention groups similar reduction of lobular inflammation and ballooning degeneration was observed. This data accompanied with significant but more pronounced reduction of proinflammatory cytokines (IL)-1$\beta$, IL-12Bp40, INF-$\gamma$) and restoration of anti-inflammatory cytokines (IL-4, IL-10, TGF-$\beta$) levels for combination of probiotic with omega-3.
**Conclusion:** Combination of alive probiotic with omega-3 are superior in NAFLD prevention and lead to greater reduction of liver triglyceride accumulation as compared to probiotic alone.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0531 IMPACT OF BODY MASS INDEX AND BODY COMPOSITION ON LUNG FUNCTION IN ADULT PATIENTS WITH CYSTIC FIBROSIS AFTER LUNG TRANSPLANTATION

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**Introduction:** Cystic fibrosis (CF) is a multisystem disease mainly affecting the gastrointestinal and respiratory tract. Nutritional status (NS) is an important prognostic factor and has been shown to correlate with lung function prior to

lung transplantation (LT). The impact of malnutrition and vitamin D deficiency on lung function after LT is unclear.
**Aims & Methods:** This study aimed at investigating the impact of body mass index (BMI), body composition (BC), and vitamin D – levels on lung function in adult CF patients after LT. Therefore, consecutive adult CF patients after LT who attended our CF outpatient service between January 2012 and July 2015 were included. Data on BC measured by 3 compartment model bioelectrical impedance analysis (BIA), general nutritional status as evaluated by BMI, as well as 25-hydroxy(OH)-vitamin D levels at initial visit and follow-ups were collected retrospectively and correlated with lung function parameters.
**Results:** In total, 58 patients (59% female, median age: 30.1 y) were included. The majority (81%) carried the F508del allele, were pancreatic insufficient (PI; 97%), diabetics (80%; CFRD or NODAT), or had reduced bone density (88%). Median BMI was 19.6 $kg/m^2$. More than a quarter of subjects (16/58; 28%) were malnourished (BMI < 18.5 $kg/m^2$), none of the patients was classified as obese. BMI significantly correlated with lung function. Malnourished patients had significantly reduced lung function compared to normal/overweight patients. BMI, as well as the single BIA parameters PA, TBW, FFM, and BCM were univariate predictors of lung function as assessed by FEV1%. 139 BIAs performed in 58 patients during longitudinal follow-up were analysed, demonstrating a steady rise in median BMI, PA and BCM. In parallel lung function fell slowly, but constantly during the same period (FEV1% from 88% to 80.5%). In malnourished patients, a dramatic reduction of −43% in FEV1% was observed in the longitudinal term, whereas the FEV1% decline in the normal/overweight patients was only −4%. Vitamin D deficiency was highly prevalent but was not associated with lung function after transplantation.
**Conclusion:** BMI, PA, TBW, FFM, and BCM in contrast to vitamin D levels are univariate predictors of lung function in adult CF patients after LT. Diabetes (CFRD or NODAT) and vitamin D deficiency are highly prevalent in post-transplant CF patients. Malnourished patients had significantly impaired lung function within the longitudinal follow – up. Continuous care by a multidisciplinary and specialized team of dietitians and gastroenterologists trained in CF care might improve nutritional status in CF patients after LT.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0532 COMORBID FUNCTIONAL DYSPEPSIA AND PSYCHOLOGICAL SYMPTOM SEVERITY ARE INDEPENDENTLY ASSOCIATED WITH HIGHER GASTROINTESTINAL SYMPTOM SCORES AFTER A LACTULOSE NUTRIENT CHALLENGE TEST IN IBS

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**Introduction:** Irritable Bowel Syndrome (IBS) is associated with an increased postprandial symptom response to a lactulose nutrient challenge test (LNCT) compared to healthy controls. Co-morbid Functional Dyspepsia (FD) and psychological comorbidity are highly prevalent in IBS, but are not regularly taken into account. Our aim was to investigate the association between co-morbid FD status and severity of co-morbid psychological symptoms on the one hand and the symptom response to the LNCT in IBS and healthy controls.
**Aims & Methods:** 205 IBS patients (Rome III), 94 (46%) of whom had co-morbid FD (IBS-FD, Rome III), and 83 healthy volunteers (HV) consumed a 400-ml liquid breakfast (NutridrinkÒ) combined with 25 g of lactulose after an overnight fast. They completed graded rating scales (0–20) assessing severity of gastrointestinal (GI) symptoms (abdominal pain, bloating, nausea, gas, urgency) and overall ''digestive comfort'' before breakfast and every 15 minutes up to 240 minutes, postprandially. The relationship between subject health status (HV, IBS, IBS-FD) and the course of GI symptom scores over time were analyzed using linear mixed models with level of anxiety, depressive, and somatization symptoms as continuous covariates.
**Results:** A significant main effect of group, (i.e. difference between the three groups in the average symptom level over time), was found for all symptoms (all $p < 0.0001$). Post-hoc tests showed that both IBS groups differed significantly from HV for all symptoms, whereas IBS-FD had higher levels of bloating ($p_{Tukey} = 0.004$), abdominal pain ($p_{Tukey} = 0.005$), and digestive comfort ($p_{Tukey} < 0.01$) compared to IBS. A significant group-by-time interaction effect was found for bloating ($p = 0.009$), abdominal pain ($p = 0.0006$), urgency ($p = 0.049$) and digestive comfort ($p = 0.002$). A significant difference in symptom increase from baseline between IBS-FD and IBS was found in abdominal pain ($p_{FDR} = 0.013$). In addition, anxiety levels were positively associated with symptom levels for all symptoms (all $p < 0.025$) except abdominal pain, levels of which were associated with somatization severity ($p < 0.0001$). Breath test results ($H_2$ and $CH_4$) were not different between groups, yet anxiety levels were positively associated with hydrogen levels ($p < 0.0042$).
**Conclusion:** In IBS, co-morbid FD is associated with increased GI symptom reporting, both preprandially and after a LNCT, particularly for abdominal pain, and is associated with decreased overall digestive comfort reporting. Anxiety and somatization have independent additional effects. These results indicate that the presence of co-morbid FD and levels of psychological symptoms are relevant for symptom reporting in IBS, including after a lactulose nutrient challenge test.
**Disclosure of Interest:** D. Pohl: Daniel Pohl has served as Consultant for Astra Zeneca, Allergan and Takeda and as Speaker for Allergan, Almirall, Astra Zeneca, Sucampo and Takeda.
H. Törnblom: Hans Törnblom has served as Consultant/Advisory Board member for Almirall, Danone and Shire.
B. Le Nevé: Boris Le Nevé is employed by Danone Research.
J. Tack: Jan Tack has served as Consultant/Speaker for: Abbott, Almirall, AlfaWasserman, AstraZeneca, Danone, Janssen, Menarini, Novartis, Nycomed, Ocera, Ono pharma, Shire, SK Life Sciences, Theravance, Tranzyme, Xenoport, Zeria Pharmaceuticals.
M. Simrén: Magnus Simrén has received grants from Danone, and Ferring Pharmaceuticals, and served as a Consultant/ Speaker for Albireo, Allergan, Almirall, Astra Zeneca, Danone, Glycom, Chr Hansen, Nestlé, Shire, Takeda and Tillots.
All other authors have declared no conflicts of interest.

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## P0533 PROTON PUMP INHIBITORS – A RISK FOR MICRONUTRIENT DEFICIENCY. BUT ARE WE LOOKING OUT FOR THIS?

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**Introduction:** Proton pump inhibitors (PPIs) have long been established as an effective evidence-based therapy for many upper gastrointestinal diseases including peptic ulcer disease, gastro-oesophageal reflux disease, oesophagitis and dyspepsia. However, nonjudicious use of PPIs creates both preventable financial as well as medical concerns. There are several studies that point to potential micronutrient deficiencies including iron, vitamin B12, magnesium and calcium as a consequence of long-term PPI use. While these risks are considered to be relatively low in the general population, they may be notable in elderly and malnourished patients on PPIs. Although high-quality evidence for the true burden of deficiency is scarce, clinicians should have an awareness of the potential for these side effects in patients, particularly those on long-term PPIs.
**Aims & Methods:** We hypothesised that despite increasing evidence of micronutrient deficiency in patients on long-term PPIs, this is not assessed in clinical practice. A single-centre, retrospective analysis of all patients on long term PPIs usage in a large NHS North London trust was performed. Patients with Barrett's oesophagus were used as a database of patients on long-term PPIs. Their names were identified from the Unisoft endoscopy reporting system as undergoing endoscopic surveillance for Barrett's. We reviewed their electronic patient records to see if they had ever had their indices for B12, ferritin or magnesium tested whilst they had been undergoing outpatient clinical review.
**Results:** Of 41 patients identified, 38 (92.7%) had not had serum magnesium checked in the last 12 months including 15 (36.59%) who had never had it checked. 32 (78.1%) had not had serum ferritin or B12 checked in the past 12 months. Including 9 (21.95%) whom had never had it checked. The median magnesium level was low (0.77, range 0.76–0.89). The median ferritin was normal (106, range 13–196). There was one incidence of B12 deficiency (2.44% all patients, 31.3% of all those tested). Median serum B12 was normal (351, range 10.6–645).
**Conclusion:** Despite evidence in the literature of an association between long term PPI use and micronutrient deficiency, the investigation for this by clinicians in a high-risk group was poor and inconsistent. Even in this small cohort, magnesium and B12 deficiency was detected. We would recommend that clear guidance from national Gastroenterology bodies on micronutrient monitoring in patients on long term PPIs is required. This may improve screening of micronutrients in long term PPI usage and identify those requiring supplementation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0534 A CROSS-SECTIONAL STUDY ON THE MILK CONSUMPTION IN SOUTHERN ITALY

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**Introduction:** Milk consumption has had a sharp decline in the last decades, particularly in developed countries**.** One of the reasons for this decline is the diagnosis or the perception of lactose intolerance**.**
**Aims & Methods:** Our aim was to investigate average milk and dairy products consumption in Campania (Italy), one of the main producers of Italian dairy products. Subjects, aged 18–75 years and lived in Campania, were invited to answer an online questionnaire on the average milk and dairy products consumption posted on the public-access Hospital website, and on several Facebook pages

of friends and hospital personnel. The survey consisted of 16 questions and we calculated an average time of 5 minutes to complete it. Categorical variables were expressed as frequency and differences in frequencies between groups were calculated using $\chi 2$ test. Covariates included sex, age (18–35, 35–49, 50–75), body mass index (BMI kg/m$^2$), classified as underweight ($\leq$18.5), normal weight ($>$18.5–25), overweight ($>$25–30) and obese ($>$30), job type (classified as student, housewife, low, middle and high class job based on the average salary, retired and unemployed) and physical activities based on the weekly physical activity. We used logistic regression models to evaluate the influence of each covariate in the milk habit. All ORs were adjusted for sex, age, BMI, job and physical activities when not stratified for.
**Results:** We included in our analyses 1173 questionnaires. Most of the subjects were females (66%), aged 18–34 years (44.9%), had a high-class job (44.7%) which included university professors, managers and doctors and 42.4% of them did not practice any sport. We showed that 22.2% (260/1173) of responders from Campania population does not drink fluid milk, and 18.1% (213/1173) drinks lactose-free milk, mainly because of gastrointestinal symptoms. We considered two groups: group 1, people who drink fluid milk (with and without lactose) and group 2, those who do not drink milk. There were more women than men (OR 1.40, 95% CI 1.02–1.92) and less people aged 50–75 years than 18–34 years (OR 0.56, 95% CI 0.38–0.84) in group 1 compared to group 2. Moreover, a sub-analysis showed that females and underweight people drink more lactose-free milk than milk with lactose. Considering the dairy products, only 7 (0.6%) persons among our population do not regularly eat dairy products, while 86.7% of them eat these products at least once a week. Most of the people in our cohort avoid drinking fluid milk because of gastrointestinal symptoms without any doctor advice. Five subjects instead believe that milk and any dairy products are dangerous and can cause cancer; fifteen subjects do not drink fluid milk as they do not like it, eight because they are on a diet, and think that milk is a fat product.
**Conclusion:** The decrease in fluid milk consumption, a low-cost source of proteins, is considered a public health problem that deserves a strategy to raise. In fact, the trend of decreased milk consumption and the parallel increased consumption of cheese means the greater intake of cholesterol and calories. Our data support the need of a mandatory implement of the nutritional campaign to avoid unnecessary fluid milk avoidance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0535 NUTRITIONAL DEFICIENCIES IN PATIENTS WITH CHRONIC ATROPHIC AUTOIMMUNE GASTRITIS


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**Introduction:** Chronic atrophic autoimmune gastritis (CAAG) is characterized by the presence of autoantibodies against gastric parietal cells or intrinsic factor and a progressive destruction of the parietal cells, leading to hypo/achlorhydria responsible for a reduced absorption of vitamin B12. A possible role of CAAG and gastric achlorhydria in the pathogenesis of multiple nutritional deficiencies, including vitamin C, folic acid, vitamin D and calcium, has been reported.
**Aims & Methods:** Present series was aimed at evaluating both the prevalence of nutritional deficiencies in CAAG patients and the potential relationship with the grading of gastric atrophy or enterochromaffin-like (ECL) cells hyperplasia or body mass index (BMI). From January 2005 to January 2016 122 consecutive CAAG patients (100 F; median age 65 years, range 25–90) underwent regular follow-up with annual blood tests and upper gastrointestinal tract endoscopy every 3 years. Data about BMI, blood levels of B12, 25–OH vitamin D, folic acid, ferritin, gastrin and the grading of gastric atrophy and ECL cells hyperplasia were collected in all cases.
**Results:** Of the 122 patients with CAAG, 76 (62%) presented nutritional deficiencies, single in 24 and multiple in 52 cases. In detail, a deficiency in B12 was present in 42 patients (34%; median value 130 pg/ml, range 11–190), in folic acid in six cases (5%; median value 3.4, range 2.9–4.3 ng/ml) and in iron in 42 patients (34%; median ferritin value 14 ng/ml, range 4–30). 25–OH vitamin D deficiency was present in 76 patients (62%; median value 18 ng/ml): in detail, 17 patients had vitamin D levels $<$10 ng/ml, 35 levels between 10 and 20 ng/ml and 24 levels between 20 and 30 ng/ml). Levels of 25–OH vitamin D directly correlated with blood B12 levels (p-value $<$0.05); moreover, vitamin D levels were lower in patients with macronodular ECL cells hyperplasia than in patients with linear or micronodular hyperplasia (11.8 versus 19.8 ng/ml respectively, p-value $<$0.05). No significant correlation was observed between levels of B12, folic acid or ferritin and BMI, blood gastrin levels, the grading of gastric atrophy or ECL cells hyperplasia.
**Conclusion:** 25–OH vitamin D, vitamin B12 and iron deficiencies are frequent in CAAG patients, probably because the mucosal alteration secondary to chronic autoimmune inflammation could negatively affect the absorption of the above factors. Indeed, the correlation between 25–OH vitamin D and vitamin B12 deficiency may indicate underlying shared pathogenic mechanisms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## MONDAY, OCTOBER 17, 2016 10:30–17:00
## PAEDIATRIC: UPPER GI – POSTER EXHIBITION

### P0536 CO-MORBIDITIES IN ADOLESCENTS WITH CELIAC DISEASE: FINDINGS FROM A POPULATION-BASED COHORT


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**Introduction:** Celiac disease (CD) is a systemic disorder associated with various autoimmune disorders and higher prevalence of other diagnoses and complications. The prevalence of associated diseases and complications varies in different reports.
**Aims & Methods:** We aimed to investigate the association of CD with various medical conditions at late adolescence in a large cross-sectional population-based study. A total of 2,001,353 Jewish Israeli adolescents who underwent a general health examination at median age of 17.1 (16.9–17.4) years from 1988 to 2015 were included. Of these, comprehensive data regarding medical status was available for 1,588,041 (79%) subjects. A definite diagnosis of CD was based on accepted criteria. Covariate data included demographic measures, and data on associated medical conditions.
**Results:** Overall, data of 7145 subjects with CD and 1,580,896 controls were analyzed. Multivariate analyses showed that autoimmune diseases were significantly more common in subjects with CD including insulin dependent diabetes (RR = 5.5), inflammatory bowel diseases (RR = 3.8), arthritis (RR = 2.4), thyroid diseases (RR = 1.8), psoriatic skin disorders (RR = 1.6) and asthma (RR = 1.5). Further associations included bile stones (RR = 3.6), migraine (RR = 2.3), anemia (RR = 1.7), and menstrual abnormalities in females (RR = 1.5). Neither long bones fractures nor axial fractures were more common in adolescents with CD compared with controls.
**Conclusion:** Already at adolescence, CD is associated with multiple comorbidities, not limited to autoimmune disorders.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0537 ETHNIC DISPARITIES IN PHENOTYPE AND HISTOPATHOLOGY PROFILE IN CHILDREN WITH CELIAC DISEASE


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**Introduction:** The prevalence of Celiac Disease (CD) has increased dramatically worldwide with a high variability in the clinical presentation. Despite the relationship between a common genetic heritage and the phenotype of the disease, the contribution of racial disparities in pediatric CD is unclear.
**Aims & Methods:** To investigate a possible association between ethnicity and clinical presentation, familial occurrence of CD and histological severity of the disease. Data were retrieved from questionnaires, distributed via mail by the Israeli Celiac Foundation, and medical charts in two academic medical centers in Israel. We compared demographics, clinical presentation at diagnosis, laboratory results, familial occurrence of CD, additional autoimmune diseases and histological severity of CD by Marsh classification in the four ethnic groups to determine any association between these parameters to ethnicity.
**Results:** Data from 1223 children with CD, 41% males, 237 Ashkenazi, 110 Sheparadi, 360 mixed origin and 517 Bedouins, were requited. Familial occurrence of CD and the presence of additional autoimmune diseases were similar between the four different ethnic groups. Atypical symptoms such as anemia or elevated liver enzymes were reported in 47% of children. Despite anemia at presentation that was more prevalent among Bedouin children (p = 0.01 l) clinically they had less intestinal symptoms like abdominal pain, diarrhea, vomiting or failure to thrive (P = 0.011). Histological severity of CD by Marsh classification (Marsh 3C) was higher in the Bedouin origin. Multivariate logistic regression analysis revealed that only presence of anemia and Bedouin origin were associated with more advanced disease [OR of 2.03 (95% C.I 1.31; 4.308) (p $<$ 0.009) and OR 1.78 (95% C.I 1.31; 4.308) (p $<$ 0.003) respectively].

**Conclusion:** CD in Bedouin children has different clinical phenotype with more severe histological disease at presentation. These differences might be explained by variable environmental cultural and nutritional factors in the Bedouin group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0538 ANTHROPOMETRIC MEASURES AND PREVALENCE TRENDS IN ADOLESCENTS WITH CELIAC DISEASE: A POPULATION-BASED CROSS-SECTIONAL STUDY

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**Introduction:** Celiac disease (CD) occurs in about 1%-3% of the population, in most countries, with a recent reported increase in prevalence. Data regarding anthropometric measures in adolescents with CD, particularly final adult height, is inconclusive and mostly relies on relatively small cohorts.
**Aims & Methods:** We aimed to investigate anthropometric measures including height at late adolescence in a large National cohort. In addition we assessed trends in the prevalence of diagnosed CD over time and impact of socio-demographic factors. Between 1988 and 2015, most of the Jewish population of Israeli adolescents ($n = 2{,}001{,}353$) underwent a general health examination at a median age of 17.1 (16.9–17.4) years. A definite diagnosis of CD was based on accepted criteria. Covariate data included demographic and anthropometric measures.
**Results:** Overall, 10,566 CD cases were identified and analyzed. Multivariate analysis demonstrated that males with CD are leaner (BMI $21.2 \pm 3.7$ vs. $21.7 \pm 3.8$, $p = 0.02$) while females with CD are shorter ($161.5 \pm 6$ vs. $162.1 \pm 6$, $p = 0.017$) than the general population. The prevalence of diagnosed CD increased from 0.5% to 1.1% in the last 20 years with a female predominance (0.64% vs 0.46%). CD prevalence was significantly lower in subjects of lower socioeconomic status and those of African, Asian and former Soviet Union origin ($p < 0.0001$).
**Conclusion:** Adolescent males with CD are leaner and females with CD are shorter compared with the general population. However, the clinical relevance of the small differences suggests that when CD is diagnosed during childhood, final weight and height are not severely impaired. Our cohort reinforces the observed increase in diagnosed CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0539 CLINICAL PRESENTATION OF CELIAC DISEASE AND ESPGHAN CELIAC DISEASE GUIDELINES RETROSPECTIVE REAL-TIME APPLICATION IN A SINGLE-CENTER EUROPEAN PEDIATRIC POPULATION: A 10 YEARS EXPERIENCE

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**Introduction:** Celiac disease (CD) is a chronic illness characterized by an immunoreaction to gluten peptides that results in a small bowel enteropathy. Its incidence is increasing in the last decades from 1% to 3% of children (1,2). This increase may be related to different factors: the adoption of new criteria for diagnosis, a major awareness of the disease by physicians and a wider laboratory screening extended also to asymptomatic subjects that are at high-risk for CD (3–6). Besides the increasing incidence, changes in the clinical presentation have been observed since the 1980s: instead of the classical symptoms, atypical symptoms have been increasingly noticed (7).
**Aims & Methods:** The aim of the present study was to retrospectively investigate CD clinical presentation at diagnosis in a children Italian population from 2004 to 2014. We also retrospectively applied new ESPGHAN criteria to our population in order to quantify the number of endoscopy avoidable. We considered all pediatric patients referred as Gastroenterology outpatients to the Pediatric Unit of Modena Hospital with a suspicion of CD. All demographic, clinical, laboratory and endoscopy data were recorded. We searched for differences of symptoms presentation for CD in the period 2004–2009 vs 2009–2014 and if there were relationships between IgA-tTGA (tissue transglutaminase) levels and Marsh grade degree at biopsy with debut symptoms of CD. Then, we classified our patient according to the new ESPGHAN criteria for CD diagnosis in order to obtain the number of CD patients correctly identified by new criteria.
**Results:** We collected data of 360 patients: 7 patients were excluded for incomplete data, 48 patients were diagnosed of CD without biopsy according to the new ESPGHAN criteria, 43 patients had asymptomatic CD and were evaluated because at high-risk for CD. The comparison between 2004–2009 and 2009–2014 documented no difference ($p = 0.177$) as far as the frequency of either symptomatic (both classical and non-classical onset of the disease) or asymptomatic CD is concerned. In particular, at specific symptoms level, asthenia was predominantly reported in the second period (2009–2014) ($p = 0.02$), the association with atopic dermatitis in the first one ($p = 0.05$). Frequent changes in bowel habits were present more frequently in patients with a low-degree of mucosal damage (Marsh 2 vs 3) ($p = 0.30$). Lack in appetite was correlated with higher IgA-tTG levels ($p < 0.01$). IgA-tTG levels were strongly correlated with Marsh grade and the differences among Marsh grade were statistically significative ($p < 0.001$). Applying new ESPGHAN criteria to our population all patients were correctly classified and the number of endoscopy possibly avoidable was 98/353 (27.8%).
**Conclusion:** In the last decade the clinical onset of celiac disease did not change in our population. Classical gastrointestinal symptoms were correlated with the degree of bowel mucosa damage according to Marsh grade and IgA-tTG levels, that were confirmed to be related. Almost one third of endoscopy could be avoided in our population according to the new ESPGHAN criteria.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0540 SMALL INTESTINAL BACTERIAL OVERGROWTH AMONG CHILDREN WITH GASTRO-ESOPHAGEAL REFLUX AND NONCELIAC GLUTEN SENSIVITY

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**Introduction:** Non-celiac gluten sensitivity (NCGS) is characterized by intestinal symptoms (bloating, diarrhoea and abdominal pain) compatible with irritable bowel syndrome (IBS) that occurs after ingestion of gluten in subjects in whom infectious enterocolitis, inflammatory bowel diseases, celiac disease and wheat allergy have been ruled out. Gastro-esophageal reflux disease (GERD) is mainly a functional condition often diagnosed in children and treated with proton pump inhibitors (PPI). Long term PPI can alter intestinal bacterial population by suppressing the gastric acid barrier and may cause diarrhea.
**Aims & Methods:** The aim of this study was to evaluate the incidence of small intestinal bacterial overgrowth (SIBO) assessed by glucose hydrogen breath test (GHBT) among children that received 12 weeks of PPI treatment with or without probiotics associated, compared to children with NCGS that did not received PPI and a control lot. Methods: We performed GHBT to 182 consecutive children aged 1–18 years old: 64 with GERD who received PPI for 12 weeks, 58 children with NCGS in absence of PPI treatment and 60 healthy control subjects. The children with GERD were randomized in two groups: 32 who received only PPI and 32 who received PPI and probiotics (Lactobacillus reuteri) for 12 weeks. In children with GERD, GHBT was performed before treatment and after 12 weeks of treatment for every child.
**Results:** There weren't any was no patient detected with SIBO by GHBT among children with GERD before treatment. After 12 weeks of treatment, we detected SIBO among 56% of children treated with PPI only (18/32), compared to 6% of children treated with PPI and probiotics (2/32), ($p < 0.001$). SIBO was detected in 20% of patients with NCGS (12/58) and 5% of healthy control subjects (3/60). There was a statistically significant difference regarding SIBO prevalence between children with GERD treated with PPI only and those with NCGS or healthy control subjects ($p < 0.001$). Children with GERD treated with PPI and probiotics had a significant lower prevalence of SIBO, similar to control lot.
**Conclusion:** SIBO assessed by GHBT occurred more frequently among children with GERD treated with long-term PPI compared to children with NCGS or control subjects. Association of probiotics based on Lactobacillus reuteri decreased the rate of SIBO among children with GERD treated with PPI. Being a functional disorder that request long term PPI, GERD may benefit by acid suppression inhibition combined with probiotics in order to decrease the risk of intestinal bacteria alteration.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0541 LINKED COLOR IMAGING COMBINE MAGNIFY ENDOSCOPY FOR HELICOBACTER PYLORI INFECTION AND INTESTINAL METAPLASIA: A PIONEER STUDY WITH PRELIMINARY RESULT IN TAIWAN

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**Introduction:** LCI as a novel image-enhanced endoscopy has been reported usefully in *H. pylori* infection diagnosis. Since, H. pylori is one of the carcinogen of gastric cancer and also related to gastric or duodenal ulcer. We expect that LCI combine magnify endoscopy can increase diagnosis rate of H.pylori infection
**Aims & Methods:** The aim of this study is to evaluate the usefulness of LCI combine magnify endoscopy for diagnosis of H. pylori infection. We conduct a prospective study enrolled 52 patients from June 2016 to April 2016 at Chang Gung Memorial Hospital, Linkou medical center, Taoyuan, Taiwan. We use at least 2 methods to make sure of H. pylori infection. The procedures were performed only by one experience endoscopist. The specimens are checked by two experience pathologist.
**Results:** The accuracy diagnostic rate of H. pylori infection in LCI/Magnify endoscopy/Combine group were: 78.5%/83.6%/92.3%. The accuracy diagnostic rate of intestine metaplasia was 72.4%
**Conclusion:** LCI is a useful tool for diagnosis of H. pylori infection and intestinal metaplasia when combine with magnify endoscopy. And, we can eradicate H. pylori as soon as possible once it was diagnosed. We also can arrange intensive follow up for those patients who have precancerous lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0542 HELICOBACTER PYLORI VIRULENCE GENES MAY DETERMINE CLINICAL OUTCOME AND GASTRIC PATHOLGY AMONG INFECTED EGYPTIAN CHILDREN

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**Introduction:** Different genotypes of *H. pylori* circulate in different geographic areas; the different clinical presentations are partly attributed to this high genetic diversity; however, no studies have focused on the clinical and endoscopic findings of different genotypes among Egyptian children so far.
**Aims & Methods:** To investigate the relationship between *H. pylori* virulence genes and clinical, pathologic findings and antibiotic resistance in Egyptian children with H.pylor infection: Stomach biopsies from 50 symptomatic *H.pylori* positive children (39 with hematemesis and 11with dyspeptic symptoms) and stool samples from another 50 asymptomatic *H.pylori* positive children(-controls) were tested using PCR for the presence of cagA, vacA, babA and antibiotic resistance.
**Results:** There was a significant predominance of vacA (80% vs40%), cagA (70%vs16%), and babA2 (60%vs12%) genes among cases compared to controls. The triple genotype (babA2+ cagA+ vacAs1) and type 1 (cagA+vacAs1) were prevalent in 12% and 26%of cases and absent in controls. Significant associations were found between hematemesis and babA2, cagA, vacA,triple genes and type 1, while dyspeptic symptoms were related to babA2 and cagA genes only. CagA, vacAs1m1 and type1 were associated significantly with antral nodularity and severity of inflammation,whereas vacAs1m1 and type1 were associated with presence of deep inflammation and lymphoid follicles,and cagA and type1 with active inflammation. Resistance to metronidazole was found in 36% patients,it was significantly associated to babA2 gene.
**Conclusion:** While 82% of the cases had more than one virulence genes,92% the controls had 1 gene or lacked genes completely suggesting that the virulence genes, particulary cagA and vacAs1m1 work synergistically rather than independently in causing severe pathology and severe symtopms like hematemesis. type 1genotype could be suitable for prediction of the clinical outcomes among infected Egyptian children and may be candidate for eradication therapy to prevent severe disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0543 ROLE OF THE GLUTEN-FREE DIET ON NEUROLOGICAL-ELECTROENCEPHALOGRAPHY FINDINGS AND SLEEP DISORDERED BREATHING IN CHILDREN WITH CELIAC DISEASE

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**Introduction:** Celiac disease (CD) is a systemic disorder that involves a lot of tissues, among which is the nervous system. In 2013, Diaconu [1]et al. studied the incidence of neurologic manifestations in children with CD showing that one-third of children presented one or more neurologic symptoms as the onset manifestation of CD. Status epilepticus and encephalopathy in the absence of profound GI symptom can be a symptom of a celiac crisis. A meta-analysis[2] of the few evidence-based data available on these disorders in children showed that the relative risk of epilepsy in individuals with CD, and of CD in individuals with epilepsy, compared with the general population, was 2.1 and 1.7, respectively. In the vast majority of these patients, wakefulness EEGs revealed focal abnormalities, mainly localized in one or both occipital regions.
**Aims & Methods:** To assess whether celiac children are at risk for EEG- and sleep disordered breathing (SDB), and whether an appropriate gluten-free diet (GFD) may influence these disorders. We consecutively enrolled 22 children (18 females and 5 males, mean age at diagnosis $9.51 \pm 4.17$ DS years, range 3–16 years) with a new biopsy-proven celiac disease (CD) diagnosis. At CD diagnosis and after 6 months of GFD, each patient underwent a general and neurological examination, an electroencephalogram, a questionnaire investigating neurological features, and a validated questionnaire about SDB: OSA (obstructive sleep apnea) scores $< 0$ predict normality; values $> 0$ predict OSA.
**Results:** At CD diagnosis, 8 of 22 (36.4%) patients complained headache and 3 of 22 had presented febrile seizures. 21 children filled OSAS test (mean OSAS score: $3.4 \pm 2.1$ DS). Abnormal EEG findings were observed in 11 of 22 (50%) children. The electroencephalography (EEG) examinations revealed abnormal finding, such as focal or generalized sharps and/or spikes and spike-waves, in 11 children (50%). 1 child had abnormal finding in frontal region, 3 in occipital region, 2 in parietal region and 5 children showed diffuse aberration. (Table1). After 6 months of GFD, we analyzed data of 9 children: headache disappeared in 72% of children and EEG abnormalities in 78%; all children showed negative OSA score.

| | Age at CD diagnosis | EEG abnormalities (cerebral regions) |
|---|---|---|
| 1 | 7.42 | Frontal |
| 2 | 10.33 | Occipital |
| 3 | 14.16 | Diffuse |
| 4 | 3.16 | Diffuse |
| 5 | 16.16 | Diffuse |
| 6 | 8.67 | Diffuse |
| 7 | 9.75 | Occipital |
| 8 | 0.58 | Diffiuse |
| 9 | 0.25 | Parietal |
| 10 | 6.58 | Parietal |
| 11 | 2.47 | Occipital |

**Conclusion:** According to our preliminary data, in the presence of unexplained EEG abnormalities and/or other neurological disorders/SDB in newly diagnosed CD diagnosis, is likely to be disease-related and respond to GFD over 6-month time.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0544 SMALL INTESTINAL BACTERIAL OVERGROWTH IN CYSTIC FIBROSIS: EPIDEMIOLOGY, SYMPTOMS AND A CLINICAL TRIAL WITH RIFAXIMIN

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**Introduction:** Scientific literature shows a high prevalence of Small Intestinal Bacterial Overgrowth (SIBO) in patients with Cystic Fibrosis (CF). The role of SIBO in nutritional status and gastrointestinal symptoms in CF is not known.
**Aims & Methods:** Our aim was to study SIBO epidemiology and clinical impact and to assess the efficacy of rifaximin in eradicating SIBO in CF patients. A symptoms questionnaire and Glucose Breath Test (GBT) were given to 79 patients (median age 19.6y 9.2–36.9) attending an Italian CF Centre. Subjects with a positive GBT were enrolled in a randomized controlled trial into two groups to receive oral rifaximin for 14 days or no treatment. Patients repeated GBT and symptoms questionnaire 1 month after withdrawal of therapy or 45 days after the first negative GBT.

**Results:** Twenty-five patients resulted affected by SIBO (31.6%) with a significant correlation with lower BMI ($p < 0.01$) and serum albumin levels ($p < 0.05$). Twenty-three patients took part in the randomized trial, 13 patients (56.5%) in rifaximin group and 10 patients (43.5%) in control group. Some patients dropped out for lung exacerbations. Eradication rate of SIBO was 9/10 (90%) in rifaximin group and 2/6 (33.3%) in control group ($p < 0.05$). In rifaximin group gastrointestinal symptom improvement was observed in 4/5 patients aged ≤14 years and in 0/5 patients aged >14 years ($p < 0.05$). In control group symptom improvement was observed in 2/6 patients.
**Conclusion:** CF patients show a high prevalence of SIBO, related to a lower BMI. Rifaximin therapy is well tolerated and the results are promising in terms of efficacy in relieving gastrointestinal symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0545 GASTRITIS AND HELICOBACTER PYLORI INFECTION IN CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE

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**Introduction:** There are very few studies on frequency of gastritis and *H.pylori* infection in adults with celiac disease (CD).
**Aims & Methods:** We aimed to determine the frequency of both, gastritis and H.pylori infection in children with CD. This retrospective observational multicentre study included patients diagnosed with CD at 3 tertiary pediatric gastroenterology centres in Poland: Warsaw, Bydgoszcz and Gdansk from March 2003 to March 2016. Medical records of children with new diagnosed CD were reviewed. Frequency of H.pylori infection and correlation with the presence and severity of inflammation.
**Results:** A total of 408 children were diagnosed with CD (173 males). Median age at diagnosis was 8.5 y.o. (range: 4 months – 18 years). Mean time of symptoms prior to diagnosis was 27.9 months (range: 0–156 months). Gastritis was found in 25% patients. It was more common in children with more advanced villous atrophy in duodenum (Marsh 3A vs Marsch 3C) but the difference was insignificant ($p = 0.3$). Presence of H.pylori infection was found in 8% of children and it was more frequent at younger age ($p = 0.01$). The time prior to diagnosis were not correlated with the frequency of infection ($p = 0.06$).
**Conclusion:** Gastritis is common in children with newly diagnosed CD. Time prior to diagnosis and severity of villous atrophy in duodenum are not correlated with frequency of gastritis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0546 ARE LYMPHOID FOLLICLES IN CHILDREN WITH IDIOPATHIC GASTRITIS MUCH MORE COMMON THAN PREVIOUSLY THOUGHT?

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**Introduction:** The rate of *Helicobacter pylori* positive (Hp+) gastritis has been declining over the years. As a result, *Helicobacter pylori* negative (Hp-) gastritis has become more prevalent. While the presence of chronic gastritis and IM in children with *H. pylori* has been well studied, there is very little data regarding the risk factors, clinical and histological characteristics of non *H. pylori* induced chronic gastritis and IM in the pediatric literature.
**Aims & Methods:** We therefore attempted to evaluate the prevalence, risk factors, and clinical correlations of chronic gastritis and IM in childhood, and it's relation to *H. pylori* infection and celiac disease in all patients who had gastric biopsies performed at our medical center over a one-year period.
The medical records of children aged between 1 and 18 years that underwent elective esophagogastroduodenoscopy at Assaf Harofeh Medical Center in Israel were retrospectively reviewed. Demographic, clinical, endoscopic and histologic features were analyzed. Gastric biopsies were taken from the antrum and from the corpus and graded using the Updated Sydney System. Hp+ gastritis was defined by the presence of *H. pylori* by histology (H&E, Gimsa or immunohistochemistry staining).
**Results:** A total of 184 children met the study criteria (61.9% girls) with a mean age of 10 years. Out of 184, 66.3% (122) had chronic gastritis; of these 60.7% (74) had Hp- gastritis. Children with Hp- gastritis were mostly not of Arabic origin ($p = 0.011$), younger ($p = 0.003$) and presented less with abdominal pain ($p = 0.02$). The majority (95.8%) of the Hp+ gastritis children had pan-gastritis compared to only 50% in the Hp- gastritis group ($p < 0.001$). Nodular gastritis, monouclear infiltrates and neutrophils were all less prominent in Hp- gastritis compared to Hp+ gastritis ($p < 0.001$). Although less typical, lymphoid follicles were demonstrated in 51.3% of the Hp- patients. The presence or absence of celiac disease in Hp- gastritis had no impact on the histological findings.
**Conclusion:** Based on the data analyzed, we conclude that lymphoid follicles in children with idiopathic gastritis are more common than previously thought, independently of their celiac disease status. Obviously, additional long term follow-up studies in those young patients should help clarify the importance of this process, facilitate identification, surveillance and treatment strategies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0547 FRUCTOSE SENSITIVITY – AND NOT FRUCTOSE MALABSORPTION – CORRELATE WITH THE CLINICAL SYMPTOMS REPORTED BY CHILDREN WITH CHRONIC ABDOMINAL PAIN?

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**Introduction:** Fructose malabsorption is generally considered as a possible cause of chronic abdominal pain in children. Fructose malabsorption can be determined with the fructose breath hydrogen test (BHT). However, fructose malabsorption and abdominal symptoms do correlate poorly.
**Aims & Methods:** Our aim was to evaluate whether fructose malabsorption or rather fructose sensitivity correlates with clinical symptoms in children with chronic abdominal pain. 60 patients (age: 10–15 years; 28 male, 33 female) with chronic abdominal pain received a fructose BHT for clinical suspicion of carbohydrate induced gastrointestinal symptoms. Clinical symptoms were quantified by a faces graded scale (0 = no symptom, 5 extreme symptom) evaluating severity of pain, nausea, meteorism, flatulence and diarrhea in the 4 weeks before the BHT. An overall 4weeks symptom score was calculated by adding each single score. For the BHT subjects ingested a 20% fructose solution, 1 g/kg body weight up to a maximum of 25 g. An increase of breath hydrogen concentration by at least 20 ppm over baseline was considered to demonstrate malabsorption. Symptoms during the BHT were ascertained regularly up to 9 hours after commencing the test on a faces graded scale. Fructose sensitivity was defined as one or more symptoms increasing significantly (2 points or more) over baseline. Median ($25^{th}/75^{th}$ percentile) are given, $p < 0.05$ was considered significant.
**Results:** 23 out of 60 were fructose malabsorbers, 21 patients (13 m, 8 f) turned out to be fructose sensitive. Among the fructose malabsorbers, 11 were fructose sensitive and 12 had no increased symptoms during the BHT. Overall 4 weeks symptom score was 6.0 (3.5/8.5) in malabsorbers and 5.5 (1.75/7.5) in non-malabsorbers (NS). In contrast, the overall 4 weeks symptom score of fructose sensitive patients [9.0; (5.5/13.0)] was significantly higher than that of non-sensitive patients [4.0; (1.5/6.0)] ($p < 0.001$), independent whether they malabsorbed fructose or not. No individual symptom differed in fructose malabsorbers and absorbers in the 4 weeks before the BHT, while pain ($p < 0.01$), meteorism ($p < 0.001$), flatulence ($p < 0.001$) and diarrhea ($p < 0.001$) was significantly more severe in fructose sensitive patients as compared to non-sensitive subjects.
**Conclusion:** Fructose sensitivity, but not fructose malabsorption, correlates well with clinical symptoms in children with chronic abdominal pain.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0548 HOW DO THE MATERNAL AND NEWBORNS PARAMETERS INFLUENCE THE CHILDREN'S BIRTH WEIGHT?

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**Introduction:** The birth weight is determined by maternal and neonatal factors and it influences the afterwards child's nutritional status.
**Aim** – to evaluate the maternal and neonatal factors that influence birth weight.
**Material and method** – We performed a prospective study on 151 mothers and 151 de newborns in a tertiary center maternity from Romania. We evaluated the mother's demographical factors (age, parity, smoking, educational degree); mothers' bioimpedance characteristics [Fat mass (FM), Bone mass (BM), muscle mass (MM) and total body water (TBW)]; anthropometric parameters [weight (W), height (H), body mass index (BMI), middle upper arm circumference (MUAC), tricipital skinfold thickness (TST)] and laboratory ones (cholesterol, triglyceride, ASAT, ALAT) in mothers and newborns.
**Results:** We noticed that mother's weight ($p = 0.01$), height ($p = 0.04$), gestational age ($p = 0.001$), fat mass (kg) ($27.41 \pm 6.09$, $p = 0.01$) (0.002), muscle mass (MM) ($39.09 \pm 4.87$; $p < 0.02$) and total body water ($32.48 \pm 3.82$; $p = 0.03$) influenced positively the birth weight, while mothers' smoking status was negatively correlated with birth weight ($p = 0.04$). We observed a higher incidence of mother's weight gain, and therefore a higher birth weight in the children whose mothers had superior studies ($p = 0.05$). Birth weight correlated with mother's increased TST and MUAC ($p = 0.001$). We did not identify any correlations between birth weight and laboratory parameters.
**Conclusion:** Mothers with bigger FM, MM, and TBW had children with bigger birth weight, while smoking status is negatively correlated with birth weight. Bioimpedance evaluates better pregnant women's nutritional status.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0549 TIMING OF SYMPTOMS DURING AND AFTER THE FRUCTOSE HYDROGEN BREATH TEST IN CHILDREN WITH CHRONIC ABDOMINAL PAIN

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**Introduction:** Carbohydrate malabsorption can cause visceral pain and non-painful symptoms such as nausea, meteorism, flatulence and diarrhea in sensitive patients. Fructose malabsorptioncan be determined with the fructose breath hydrogen test (BHT).

**AIM:** We evaluated the development of pain and non-painful symptoms over time in children who were referred to the fructose hydrogen breath test.

**METHODS:** 60 patients (age: 10–15 years; 28 male, 33 female) with chronic abdominal pain received for clinical suspicion of carbohydrate induced gastrointestinal symptoms a fructose BHT. Subjects ingested a 20% fructose solution, 1 g/kg body weight up to a maximum of 25 g. The diagnosis of fructose malabsorption was established when breath hydrogen concentration increased by at least 20 ppm over baseline. Symptoms during the BHT were ascertained regularly up to 9 hours after commencing the test on a faces visual analogue scale (0 = no symptom, 5 extreme symptom). Sensitivity was defined as one ore more symptoms increasing significantly (2 points or more) over baseline. Mean±SEM are given, $p < 0.05$ was considered significant.

**Results:** 21 patients (13 m, 8 f) turned out to be fructose sensitive, 39 were not fructose sensitive. Among the fructose sensitive subjects 11 malabsorbed fructose. In the non-sensitive group, 12 children were fructose malabsorbers and 27 absorbed fructose appropriately. Before fructose ingestion abdominal pain scores were low in both fructose sensitive patients ($0.60 \pm 0.2$) and non-sensitive patients ($0.87 \pm 0.2$)(NS). In the fructose sensitive group, pain scores stayed low for the following 120 min (NS vs. baseline) but increased significantly at 150 min ($1.33 \pm 0.3$; $p < 0.05$ vs. baseline). Pain resolved thereafter and did not recur. In contrast, nausea developed 30 min after baseline and continued until 120 min, meteorism was present between 120 and 150 min and urge to pass flatus was present 3 to 6 hours after fructose ingestion. Diarrhea did not develop in the fructose sensitive patients within the 9 hour observation period.

**Conclusion:** Paediatric patients with fructose sensitivity develop abdominal pain approximately 2½ hours after fructose ingestion. Other symptoms associated with fructose ingestion show distinct timing patterns.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00

**LIVER & BILIARY II – POSTER EXHIBITION**

## P0550 FACTORS ASSOCIATED WITH SIGNIFICANT LIVER STEATOSIS AND FIBROSIS AS ASSESSED BY TRANSIENT ELASTOGRAPHY IN PATIENTS WITH ONE OR MORE COMPONENTS OF THE METABOLIC SYNDROME

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**Introduction:** Diet and lifestyle changes have caused a dramatic increase in the worldwide prevalence of obesity and metabolic syndrome (MetS) in parallel with an increasing incidence of non-alcoholic fatty liver disease (NAFLD). Presence of the MetS can be used for the initial risk stratification of patients, who need further evaluation of NAFLD by using either liver biopsy or other non-invasive methods, such as the FibroScan®. However, to our knowledge, the relationship between controlled attenuation parameter (CAP), liver stiffness measurement (LSM) and MetS components has been not extensively examined in large cohorts of patients. We examined the relationship between CAP and LSM, as assessed by transient elastography (TE), and different clinical and biochemical parameters in patients with one or more components of the MetS.

**Aims & Methods:** A total of 648 consecutive patients were analyzed. The MetS was defined according to the International Diabetes Federation by the presence of at least three of the following metabolic abnormalities: waist circumference > 94 cm for men and > 80 cm for women (as a pre-requisite diagnostic criterion); blood pressure ≥130/85 mmHg or anti-hypertensive treatment; previously physician-diagnosed T2DM, or use of any hypoglycemic drugs or a fasting plasma glucose level ≥5.6 mmol/L; triglyceride levels > 1.7 mmol/L and/or HDL-cholesterol < 1.04 mmol/L for men and < 1.29 mmol/L for women or lipid-lowering treatment. CAP and LSM measurements were performed using the FibroScan® (Echosens, Paris, France) by a single experienced operator. All patients were examined using either the 3.5 MHz standard M probe or the XL probe (center frequency 2.5 MHz), depending on the body mass index (BMI) level of the patients. Significant liver steatosis was defined as a CAP value≥238 dB/m, whereas significant fibrosis was defined as a LSM value > 7.0 kPa.

**Results:** Of all analyzed patients, 82.1% had hypertension, 77.9% had atherogenic dyslipidemia, 77.5% had abdominal overweight or obesity, 45.7% had dysglycemia and 67.3% of patients fulfilled the criteria for the diagnosis of the MetS. Patients with the MetS had significantly higher values of CAP ($312.9 \pm 45.1$ vs. $278.4 \pm 50.8$ dB/m; $p < 0.0001$) and LSM ($5.8 \pm 3.3$ vs. $4.9 \pm 1.6$ kPa; $p < 0.001$) than those without the MetS. Notably, in the whole cohort, the prevalence of patients with increased CAP and LSM (as defined according to widely accepted cut-off points) were 88.3% and 16.5%, respectively. Patients with CAP≥238 dB/m (n = 572) had a markedly greater prevalence of the MetS and all its individual components. Moreover, CAP measurements increased progressively with number of MetS components ($p < 0.0001$ for the trend by one-way ANOVA). Among patients with CAP≥238 dB/m, those with LSM > 7.0 kPa (n = 103) had higher liver enzymes and a greater prevalence of the MetS and its individual components than those with LSM≤7.0 kPa. Factors independently associated with elevated CAP were presence of the MetS (or its individual components), insulin resistance, increased uric acid and LSM > 7 kPa. In multivariable logistic regression analysis, the factors that remained independently associated with LSM > 7 kPa were the presence of the MetS, diabetes mellitus type 2, hypertension, abdominal obesity, elevated HOMA-IR score and serum uric acid levels.

**Conclusion:** Patients with one or more components of the MetS have a high prevalence of NAFLD defined by TE with CAP and advanced liver fibrosis. Our data further support screening for NAFLD and/or advanced fibrosis in this group of high-risk patients. Although improvements in non-invasive assessment of liver fibrosis are still needed, we believe that transiet elastography with CAP may be a reasonable initial assessment for patients with one or more components of the MetS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0551 INVOLVEMENT OF AGE-RAGE SYSTEM FOR THE DEVELOPMENT OF HEPATIC FIBROSIS IN NASH

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**Introduction:** Metabolic syndrome such as diabetes are important pathogenetic background for the development of nonalcoholic steatohepatitis (NASH). It was reported that the expression of AGE (advanced glycation end-product) was activated in metabolic syndrome, and was also related to the development of NASH. However, precise mechanisms of AGE for the pathogenesis in NASH has not been well understood yet. We clarified the involvement of AGE-AGE receptor (RAGE) system for the development of hepatic fibrosis in NASH by RAGE gene deficient mice (RAGE KO).

**Aim:** Metabolic syndrome such as diabetes are important pathogenetic background for the development of nonalcoholic steatohepatitis (NASH). It was reported that the expression of AGE (advanced glycation end-product) was activated in metabolic syndrome, and was also related to the development of NASH. However, precise mechanisms of AGE for the pathogenesis in NASH has not been well understood yet. We clarified the involvement of AGE-AGE receptor (RAGE) system for the development of hepatic fibrosis in NASH by RAGE gene deficient mice (RAGE KO).

**Method:** Six-week-old male RAGE KO and C57BL/6 (WT) mice were fed with methionine-choline deficient (MCD) diets or control diets (NC) for 20 weeks, and evaluated the biochemical, histological and molecular analysis among these groups. In addition, signal transduction of fibrosis and AGE-RAGE system in the liver, and the crosstalk between both signals were also investigated.

**Results:** The increase of gene expression of RAGE, and remarkable hepatic steatosis and fibrosis were observed in WT mice with MCD (MCD WT). On the other hand, these phenotypes were significantly attenuated in MCD RAGE KO mice. Furthermore, hepatic triglyceride contents in MCD RAGE KO mice were significantly lower than that in MCD WT mice, even though serum triglyceride levels were not different between both groups.

Moreover, the gene expression of the fibrosis markers such as TGF-$\beta$, CTGF, $\alpha$-SMA, Type1 collagen $\alpha$1 and TIMP-1, and the inflammatory markers such as TNF $\alpha$ and NOS2 were increased in the livers in MCD WT mice. However, all of these molecules were significantly down regulated in MCD RAGE KO mice. In addition, the expression of mDia1, Egr1 and other molecules which were important downstream molecules of RAGE were increased, and ERK which was important for the activation of hepatic stellate cells was strongly phosphorylated in MCD WT mice. In contrast, the expression and the activation of these molecules were significantly attenuated in MCD RAGE KO mice.

**Conclusion:** The progression of hepatic fibrosis in NASH were remarkably attenuated by deficiency of RAGE gene. We clarified that signal transduction pathway of AGE-RAGE system through activation of mDia1, Egr1 and ERK would have important roles for the progression of hepatic fibrosis in NASH.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0552 MATRIX METALLOPROTEINASES IN NAFLD: INTERPLAY BETWEEN PLASMA, LIVER AND ADIPOSE TISSUE

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**Introduction:** (MMPs)-2 and -9 are two of the major matrix metalloproteinases (MMPs) in the circulation and are responsible for degradation of the extracellular matrix (ECM), which is composed primarily of type IV collagen. MMPs are inhibited by tissue inhibitors of metalloproteinases; being TIMP-2 the most effective inhibitor of MMP-2. MMPs have the ability to degrade ECM and their regulation through TIMPs play an important role in the pathogenesis of liver injury and adipogenesis modulation. Obesity is tightly associated with the development of Nonalcoholic Fatty Liver Disease (NAFLD) and metabolic syndrome.
**Aims & Methods:** The aim of this study is to characterize the interplay of MMPs in the different tissues related to NAFLD. 36 human samples from obese patients undergoing bariatric surgery; Plasma (P), visceral adipose tissue (VAT) and liver (L)) were analyzed. Gene and protein expression of MMP-2 and TIMP-2 were studied by qPCR and Western blot. MMP-2 and -9 activity was determined by Gelatin Zymography. Liver fibrosis and steatosis was scored according to Brunt's score or NAS.
**Results:** The highest expression (mRNA and protein) of MMP-2 and TIMP-2) was observed in VAT and Plasma, whereas in the liver the expression was much lower. Regarding the MMP-2 activitiy VAT showed the highest activity, followed by Plasma, and finally Liver. Interestingly, plasmatic MMP-2 activity showed a positive correlation with both Brunt fibrosis score and NAFLD activity score (NAS) ($p = 0.007$ and $p = 0.032$, respectively). No correlation between the MMP-2 activity in tissues (VAT and L) and liver fibrosis was evident. MMP-9 plasmatic activity did not show any significant change.
**Conclusion:** Our study demonstrate that MMP-2 gelatin activity is a good marker for assessing liver fibrosis. Since gelatin activity evaluation is easy and inexpensive, our data suggest the inclusion of MMP-2 in a future panel of biomarkers. Additionally, our data indicates that both VAT and Liver MMP-2 protein contribute importantly to plasmatic MMP2 activity and the latter represents the overall metabolic state of the patient.
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## P0553 EFFICACY OF LEPTIN PROFILE AND METABOLIC SYNDROME ON OXIDATIVE STRESS AND DISEASE PROGRESSION IN NON-ALCOHOLIC FATTY LIVER

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**Introduction:** Oxidative stress and metabolic syndrome are major contributors in the pathogenesis of nonalcoholic fatty liver disease (NAFLD). Leptin promotes oxidative stress and fibrogenesis in the liver. Therefore we aimed to evaluate the association between leptin levels, oxidative stress parameters and histopathological findings in NAFLD subjects with and without metabolic syndrome (MS).
**Aims & Methods:** Forty-two patients with no alcohol intake and with biopsy-proven diagnosis of NAFLD were studied (M/F:19/ 23; mean age $44.2 \pm 10.8$ years). Twenty NAFLD patients with MS were compared with 22 subjects without MS. The histopathological findings were evaluated as described by Brunt et al. For the determination of oxidative stress parameters malondialdehyde (MDA), and superoxide dismutase (SOD) activities were measured in serum and as well as in tissue specimens. Glutathione (GH) was measured in tissue homogenates. Nitric oxide (NO) and TNF-alpha receptor (TNF-sRp55) levels were measured in serum. Serum leptin levels were measured by radioimmunoassay. Statistical analysis was done using chi-squared test, Student's t-test, Mann-Whitney test, multivariate regression analysis and the area under receiver operating characteristic (ROC) curve. All statistical analyses were performed using SPSS® statistical software program (Ver.15.0).
**Results:** In bivariate analysis serum leptin levels didn't show any significant correlation with steatosis grade, necroinflammatory grade and stage. Serum leptin levels were neither significantly correlated with serum NO, SOD and MDA levels nor with tissue SOD, MDA and GH levels. Using serum leptin levels the ROC curve for distinguishing between NASH and NAFL didn't show any respective sensitivity and specificity (AUROC 0.48). Serum leptin levels, steatosis grade, necroinflammatory grade and stage were significantly higher in patients with MS ($p = 0.03$, 0.04, 0.004, 0.003, respectively). Patients with MS had significantly higher tissue MDA levels ($p = 0.002$, respectively), and significantly decreased tissue SOD and GH levels ($p = 0.003$ and 0.004) than those without MS. In multivariate regression analysis increase of tissue MDA (OR:1.7; %95 CI:1.02–3.95, $p = 0.035$) and serum NO levels (OR:1.6; %95 CI:1.01–4.2, $p = 0.038$) were risk factors for NASH and increase of leptin activity had preventive effect against NASH (OR:0.049; %95 CI:0.004–0.61, $p = 0.035$).
**Conclusion:** Serum leptin levels did not show any significant correlation with histological findings and oxidative stress parameters. Metabolic syndrome was associated with enhanced oxidative stress, decreased antioxidant levels, and severe histopathological changes. Patients with MS had increased leptin activity with a preventive effect against NASH. Therefore, we can postulate that metabolic syndrome in NAFLD is associated with enhanced oxidative stress and disease severity and leptin may have preventive effect against oxidative stress and against disease worsening.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0554 A CLINICOPATHOLOGICAL COMPARITIVE STUDY OF LEAN VERSUS OVERWEIGHT/OBESE PATIENTS OF NONDIABETIC NONALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** Nonalcoholic fatty liver disease (NAFLD) refers to the accumulation of fat (mainly triglycerides) in hepatocytes that arises due to insulin resistance. NAFLD and metabolic syndrome (central obesity, hypertriglyceridemia, hypertension, impaired glucose tolerance, and low high-density lipoprotein [HDL] cholesterol) commonly coexist, with over 90% of NAFLD patients having at least one of these characteristics. A fraction of NAFLD patients (especially Asians) do not meet weight criteria of obesity. Most low BMI NAFLD patients have central obesity and are metabolically obese, which includes findings of insulin resistance.
**Aims & Methods:** The aim of this study was to compare the clinicopathological and biochemical profile of lean and overweight/obese NAFLD patients with a special emphasis on insulin resistance. This prospective study was conducted in biopsy proven NAFLD patients aged 18 to 75 years in a university hospital in India. On the basis of Asia Pacific criteria, the patients were divided into lean (BMI $< 22.99\,kg/m^2$) and overweight/obese (BMI $\geq 23\,kg/m^2$) NAFLD. Histopathological NASH was defined by NAS (NAFLD activity score) $\geq 5$. Patients with significant alcohol consumption ($> 20\,g$/day for females and $> 30\,g$/day for males), other liver diseases (hepatitis B, C or autoimmune liver disease) and diabetes mellitus were excluded.
**Results:** Among 88 NAFLD patients, 29 (33%) and 59 (67%) were in the lean and overweight/obese group respectively. The mean age was 33.31 years which was similar in both the groups. Metabolic syndrome was present in 60 (68.2%) patients. In the lean and overweight/obese group, 55.2% and 74.6% patients had metabolic syndrome respectively (p 0.06). In the lean group, the mean weight (62.76 kg, $p < 0.0001$), height (1.71 m, $p < 0.0001$), waist circumference (83 cm, $p < 0.0001$), hip circumference (89.14 cm, p 0.003), waist:hip ratio (0.93, $p < 0.0001$) was significantly lower as compared to overweight/obese group (the respective values being 71.25 kg, 1.66 m, 92.47 cm, 94.90 cm, 0.97). The median triglyceride level (190 mg/dl vs 147 mg/dl; p 0.018) and mean VLDL level (50.40 mg/dl vs 33.99 mg/dl; $p < 0.0001$) was significantly higher in the lean NAFLD group. However, the median levels of fasting serum insulin (5.57μU/ml vs 10.83μU/ml; p 0.009) and HOMA-IR (1.37 vs 2.62; p 0.010) were significantly lower in the lean NAFLD group. NASH was present in 59 patients (67%). 75.9% of the lean patients and 62.7% of overweight/obese patients had NASH (p 0.22). There was no difference in the level of ALT, AST: ALT ratio, HDL or total cholesterol in the two groups.
**Conclusion:** Most of the patients with NAFLD were males in the the 4$^{th}$ decade. Lean NAFLD patients had lower mean weight, height, waist:hip ratio. Dyslipidemia was more common in the lean NAFLD group whereas insulin resistance was less in lean NAFLD group. Metabolic syndrome and NASH were equally present in both the groups irrespective of BMI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0555 A COMPARISON OF DIAGNOSTIC PERFORMANCE OF NAFLD FIBROSIS SCORE, FIB-4 INDEX AND TRANSIENT ELASTOGRAPHY FOR THE DIAGNOSIS OF HEPATIC FIBROSIS IN PATIENTS WITH BIOPSY-PROVEN NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the western world. Early diagnosis of advanced fibrosis in NAFLD is crucial for preventing cirrhosis-associated complications. The best accurate noninvasive diagnostic tool is still under debate.

**Aims & Methods:** We aimed to compare the diagnostic performance of NAFLD fibrosis score (NFS), FIB-4 index (FIB-4) and transient elastography (TE) for the diagnosis of hepatic fibrosis in patients with biopsy-proven NAFLD. Methods: Patients with biopsy-proven NAFLD were included. Metavir score (F0–F4) was used for grading fibrosis in liver biopsy. TE was measured using the M or XL probe of Fibroscan (Echosens®, Paris, France). NFS and FIB-4 were calculated according to published formulas. Diagnostic performance of NFS, FIB-4 and TE for the diagnosis of hepatic fibrosis was calculated using the area under the ROC curve (AUROC).

**Results:** We included 105 patients, 58% men, with a mean age of $49.8 \pm 12.4$ years. Mean values of NFS, Fib-4 and TE significantly increased according to the degree of hepatic fibrosis in liver biopsy ($p < 0.001$). AUROC for the diagnosis of significant fibrosis (F2 + F3 + F4) for TE, NFS and FIB-4 were 0.809 ($CI_{95\%}$ 0.690–0907), 0.685 ($CI_{95\%}$ 0.560–0.811) and 0.662 ($CI_{95\%}$ 0.545–0.801), respectively. AUROC for the diagnosis of advanced fibrosis (≥F3) and cirrhosis (F4) for TE, NFS and FIB-4 were 0.908 (0.842–0.974), 0.852 (0.734–0.969), 0.807 (0.750–0.872) and 0.849 (0.797–0.891), 0.782 (0.675–0.889), 0.829 (0.675–0.889), respectively.

**Conclusion:** TE was the best accurate noninvasive diagnostic tool for the diagnosis of hepatic fibrosis in patients with biopsy-proven NAFLD, especially for distinguishing patients with significant liver fibrosis (≥F2). The diagnostic performance of NFS and FIB-4 did not differ significantly for the detection of significant or severe fibrosis/cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0556 NON-INVASIVE ASSESSMENT OF HEPATIC FIBROSIS IN A SERIES OF PATIENTS WITH ALPHA-1-ANTITRYPSIN DEFICIENCY

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**Introduction:** Transient elastography (FibroScan®, FS) has been recently shown to be a valuable method in detection of liver fibrosis in adults with HBV, HCV, non-alcoholic fatty liver disease. The method seems to be promising mainly in children with liver diseases in whom indications to perform liver biopsy are very limited.

**Aims & Methods:** The aim of the study was to analyze the evaluation of FibroScan in relation to other non invasive tests of hepatic fibrosis and parameters of liver function in children with portal hypertension due to alpha-1-antitrypsin deficiency (ATD PiZZ) compared to ATD patients without portal hypertension, heterozygotes of ATD and healthy controls. We investigated 6 children with ATD PiZZ and portal hypertension aged 3.3(0.8–10.3) y [med (min-max)], 31 asymptomatic PiZZ ATD aged 5.8(1.5–17.9), 8 heterozygotes in ATD (7 PiMZ and 1 PiSZ) aged 5.3(0.8–12.3) and 16 healthy controls aged 6.8(0.4–12.8). Liver function parameters, abdominal ultrasound exam with Doppler and transient elastography were performed in ATD patients. AST/platelet ratio index (APRI), GGTP/platelet ratio index (GAPRI) and FIB-4 index were calculated in ATD groups.

**Results:** Increased liver stiffness in elastography was found in the ATD PiZZ group with splenomegaly compared to ATD without splenomegaly ($p = 0.0001$) and in ATD PiZZ with splenomegaly compared to heterozygotes ($p = 0.002$). Both APRI and GAPRI, but not FIB-4 were significantly higher in the ATD group with splenomegaly compared to ATD group without splenomegaly and ATD heterozygotes.

**Conclusion:** For the first time FibroScan values were assessed in children with liver disease due to alpha-1-antitrypsin deficiency and seem to be clinically useful for predicting liver fibrosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0557 ASSESSMENT OF CHANGE OF INTRAHEPATIC FAT AMOUNT USING CONTROLLED ATTENUATION PARAMETER IN CLINICAL TRIAL

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Introduction:
Multi-echo modified Dixon (mDixon) sequence (MR-PDFF) is a safe and non-invasive alternative for the quantification of hepatic fat content. And it has accepted reasonable method to assess the change of hepatic fat amount in phase II study. Recently controlled attenuation parameter (CAP) has been showed good correlation with intrahepatic fat amount compare to liver biopsy as well as MRS data in large cross sectional cohort. However there is little known whether change of CAP scores can be used in clinical trial. We investigated the correlation with CAP and MRS by serial examination in clinical trial setting.

**Aims & Methods:** Sixty-five NAFLD patients were evaluated with MRS and transient elastography including CAP in clinical study. Both MRS and CAP were evaluated after three month probiotic clinical trial in patients with NAFLD.

**Results:** Baseline CAP and MR-PDFF showed good correlation assessing hepatic steatosis ($r = 0.60$, $p < 0.001$). Also, changes of CAP value was also correlated with changes of intra-hepatic fat % using MR-PDFF ($r = 0.35$, $p = 0.008$) in clinical trial setting. Concordance rate of improvement or aggravation was comparable in both two methods. However, the less change amount was small in CAP value, the less concordance rate showed more weak with MR-PDFF. When the change of CAP value after treatment was less than 20, concordance rate with MR-PDFF was decreased to 15/25 (60%).

**Conclusion:** CAP and MRS have a comparable diagnostic value for the hepatic steatosis quantification as well as assessing changes of hepatic fat amount in clinical trial. However, a careful interpretation of the steatosis change using CAP score should be given when the absolute change value was less than 20 in clinical trial setting.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0558 USING OPTICAL METABOLIC IMAGING TO INVESTIGATE MECHANISMS OF PARACETAMOL INDUCED HEPATOXICITY

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**Introduction:** Paracetamol is the most readily available and widely used painkiller. However, its toxicity remains the most common cause of liver injury. The toxicity of paracetamol has been attributing to its toxic metabolite, N-acetyl-p-benzoquinoneiminie (NAPQI), which could deplete cellular glutathione (GSH) stores and react within cells to increase oxidative stress, leading to mitochondrial dysfunction and cell necrosis.[1] To better understand mechanisms of paracetamol induced liver injury, optical metabolic imaging (OMI) were used to define optical redox ratio of NADH and FAD and in cells in this study to represent the relative rates of glycolysis and oxidative phosphorylation within cells.[2,3] Multiphoton microscopy (MPM) and fluorescence lifetime imaging (FLIM) provide quantitative imaging of biological tissues and organs in vivo and allow direct visualization of cellular events,[4] which could monitor cellular metabolism in paracetamol-induced toxicity.

**Aims & Methods:** BALB/C mice were administered a single dose of paracetamol by gavage. After different time points, livers of mice after paracetamol overdose were collected for MPM-FLIM imaging. The optical redox ratio of liver tissues was calculated using NADH fluorescence intensity divided by FAD fluorescence intensity at pixel to create a redox ratio image. The average fluorescence lifetime of NADH ($\tau$m) of livers was recorded at excitation of 740 nm and emission wavelength of 350 to 450 nm. GSH depletion was measured in different zonations of the liver using mBBr dye for detection of GSH levels. Finally, serum alanine aminotransaminase (ALT) activity was measured and liver tissues were collected for histological examination and necrosis cells were quantified in different zonation.

**Results:** High-resolution images allowed visualization of cellular morphology and cell variability of the optical redox ratio and NADH fluorescence lifetimes in hepatocytes from normal and paracetamol overdose groups. Compared to normal mouse liver, average fluorescence lifetime of NADH and redox ratio of hepatocytes was significantly decreased after paracetamol overdose for 12 and 24 h, reflecting impaired metabolic activity after paracetamol treatment. Furthermore, morphological changes observed in MPM images were consistent with conventional histological results. GSH levels of treatment groups were significantly lower than those of normal livers, with gradually decreasing from periportal to centrilobular zonation. The redox status and NADH fluorescence lifetime altered prior to the changes of ALT activity and cell morphology.

**Conclusion:** Cellular metabolism changes prior to paracetamol-induced cell necrosis. Optical metabolic imaging has significant implications for investigating metabolic mechanisms of paracetamol toxicity.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0559 A NOVEL IN VITRO TEST IMPROVES CAUSALITY ASSESSMENT OF DRUG INDUCED LIVER INJURY IN PATIENTS WITH POLYMEDICATION


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**Introduction:** Drug-induced liver injury (DILI) is the major cause for acute liver failure in developed countries and accounts for a significant number of drug withdrawals and restrictions of use. However, the idiosyncratic form of DILI (iDILI) is a very challenging diagnosis. In polymedicated patients the identification of the causative agent may be impossible (1,2,3). We have developed a method that makes use of hepatocyte-like cells derived from peripheral blood (MetaHeps®) to diagnose or exclude iDILI (4).
**Aim of this study** was to investigate whether the MetaHeps® test can improve causality assessment in iDILI cases with polymedication.
**Methods:** Clinical data and blood samples were collected prospectively from patients presenting at the Liver Center Munich®, LMU university hospital with acute liver injury and intake of at least one drug with DILI concern (NCT02353455). iDILI was diagnosed by clinical likelihood(4). MetaHeps® were generated and exposed in vitro with the respective drugs. Toxicity was measured by increase in LDH release according to (4).
**Results:** As yet, 83 patients with iDILI were included in the study. In 15 cases a single drug was causing the iDILI episode (18%) while multiple drugs were involved in 68 iDILI events (82%). Seven of these patients showed iDILI at inadvertent re-exposure to one single drug (10%; 8% of total). Clinical causality assessment did not allow unequivocal identification of a single causative drug in 34 cases (50%, 41% of total). MetaHeps® testing was positive in 78 of the iDILI cases (94%). In the patients with positive re-exposure, the MetaHeps® test was positive for the respective drug. Positive test results for more than 1 drug were only found in 6 cases (7%; 6% of total). Interestingly, the combination of involved drugs had synergistic effects on MetaHeps® toxicity in 7 of the polymedicated patients.
**Conclusion:** In polymedicated patients with iDILI the MetaHeps® test seems to improve causality assessment. There is evidence that the test could improve causality assessment in polymedication and further the understanding of drug-drug-interactions in iDILI. Precise case characterization of iDILI events by the MetaHeps® test will help to develop drug-specific safety biomarkers.
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## P0560 THE RESPONSE OF HEPATOCYTE AND MACROPHAGE TO ETHANOL-INDUCED TOXICITY: AN IN VITRO CO-CULTURE MODEL


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**Introduction:** Macrophage migration Inhibitory Factor (MIF) is a pleiotropic cytokine involved in the pathogenesis of several acute and chronic inflammatory diseases, such as Alcoholic Liver Disease (ALD). Few information is available about MIF regulation between hepatocytes and macrophages in response to ethanol (EtOH).
**Aims & Methods:** The aim of this work is to elucidate if the cross talk between these two cell types has any effect in the hepatic inflammatory response. Co-culture (transwell system) of hepatocytes (HuH7) and differentiated macrophages (THP1+100 nM PMA) were exposed for 24 h to 25 mM EtOH; monoculture of each cell type were used as control (CTRL). We assessed the gene expression of MIF and its receptors CD74, CXCR2, CXCR4 and CXCR7 as well as TNF-$\alpha$. In order to correlate gene expression with MIF functionality we quantified the cytokine released into the culture medium.
**Results:** We confirmed that in hepatocytes, EtOH induced an up-regulation of TNF-$\alpha$. The gene expression of MIF followed the same trend of increase, even if the amount of released MIF was unchanged. The expression of CD74, CXCR2, CXCR4 and CXCR7 were barely detectable in hepatocytes, instead in macrophage monocultures exposed to EtOH did not show any changes. Interestingly, we observed that in the co-culture model only hepatocytes presented a dramatic increase in TNF-$\alpha$ gene expression, whereas macrophages presented a decrease. Moreover, in co-culture both hepatocytes and macrophages increased the release of MIF, with no changes at mRNA level. These data demonstrate that there is a synergic inflammatory response to EtOH when cells are cultured together. We also observed a significant up-regulation of CD74 (both in term of mRNA and protein expression) in co-cultured hepatocytes suggesting that cells respond differently when macrophages are present in the system. Moreover we observed that CXCR4 was very responsive, showing a strong up-regulation in co-cultured hepatocytes. The opposite pattern was observed in co-cultured macrophages, in which the mRNA expression was reduced as compared to the monoculture. No significant changes were observed for CXCR2 and CXCR7.
**Conclusion:** In conclusion, our data suggest that the hepatocyte is the target cell of the EtOH deleterious effect. These results also indicate that injured hepatocytes are able to modulate macrophages response, which once activated, contributes to perpetrate the inflammatory state by increasing the production of MIF.
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## P0561 THE PROTECTIVE EFFECTS OF HELIX B SURFACE PEPTIDE ON EXPERIMENTAL ACUTE LIVER INJURY


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**Introduction:** Erythropoietin (EPO) is a kind of endogenous protein which exerts tissue protective effects for a wide range of organs. EPO protects tissues through a heterodimer composed of EPO receptor and $\beta$-common receptor, which is pharmacologically distinct from the homodimer receptor that is known to mediate erythropoiesis. However, a very high dose of EPO is required for peripheral administration to achieve tissue protection, which consequently increases the incidence of hypertension and hypercoagulation. Therefore, a novel helix B surface peptide (HBSP) that interacts only with the heterodimer receptor has been developed, which is composed of 11 amino acids derived from the aqueous face of helix B in EPO 3D structure.
**Aims & Methods:** In this study, the protective effect of HBSP in acute liver injury (ALI) induced by carbon tetrachloride ($CCl_4$) was investigated. HBSP (8 nmol/kg) was injected intraperitoneally in C57 BL/6 mice 2 h after $CCl_4$ administration. Serum and liver tissue samples were collected on 24 h after injury. Histological injury was evaluated. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) were detected. Inflammatory cytokines was detected using real-time quantitative PCR. T cells and macrophages infiltration was examined by immunohistochemical staining. Hepatocytes apoptosis were measured by TUNEL assay and cleaved caspase-3 immunohistochemical staining. In in vitro experiment, the human liver cell line $LO_2$ was stimulated by $CCl_4$ with or without HBSP treatment. The glutathione peroxidase (GSH-Px) activity, cell survival and apoptosis were elevated. Furthermore, we examined PI3K/Akt/mTOR pathway to demonstrate the mechanism that HBSP-mediated protection in ALI.
**Results:** HBSP significantly decreased serum ALT, AST, LDH, and pro-inflammatory cytokines in liver tissues after $CCl_4$ injection compared to the $CCl_4$ group. Immunohistochemical staining indicated that the number of CD3, CD8, CD68 positive cells and the expression level of cleaved caspase-3 were significantly decreased by HBSP treatment. Besides, HBSP dramatically reduced apoptosis in vivo. In in vitro study, the activities of GSH-Px and survival rate were increased while the total apoptosis rate was reduced in HBSP-treated group compared to the control group after $CCl_4$ treatment. HBSP activated PI3K/Akt/mTOR pathway, which was confirmed by the PI3K inhibitor LY294002. Furthermore, HBSP could significantly improve the survival rate of acute liver failure mice, which could be reversed by LY294002.
**Conclusion:** HBSP is a potential therapeutic agent against $CCl_4$-induced ALI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0562 EVALUATION OF POTENTIAL FUTILITY IN ALCOHOLIC HEPATITIS – MULTICENTRE STUDY

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**Introduction:** Alcoholic hepatitis (AH) is associated with a high short-term mortality. Static and dynamic prognostic models are essential to determine the best approach to each patient.

**Aims & Methods:** We aimed to select the best potential futility criteria in patients with AH. Retrospective multicentre study including patients with AH diagnosed clinically and/or histologically admitted between January 2012 and December 2015. 28-day mortality (M28) was evaluated and Maddrey Discriminative Function (MDF), CLIF-C ACLF, CLIF-C AD, Model for End-Stage Liver Disease (MELD), MELD-Sodium, Age, Bilirubin, INR and Creatinine (ABIC), Glasgow Alcoholic Hepatitis Score (GAHS) and Child-Turcotte-Pugh(CTP) performances were compared.

**Results:** 91 patients were included (male sex:80.2%, mean age:53.4 ± 9.3 years) with a median follow-up of 20.0 months (IQR 14.0–36.0) and mean alcohol consumption of 146.2 ± 95.9 g/day. 43 (47.3%) patients were started on pentoxifylline (PTX) and 33 (36.3%) on prednisolone (PDN). There were no significant differences on Kaplan-Meier survival curves between patients treated with PDN Vs. PTX. CLIF-C ACLF was significantly superior to predict M28, namely when compared to FDM (AUROC 0.839 Vs. 0.671, p = 0.040). A CLIF-C ACLF > 60 had a positive predictive value (PPV) for M28 of 81.8%. Patients treated with PDN with CLIF-C ACLF > 60 and Lille≥0.45 had a 100% PPV for M28.

**Conclusion:** The CLIF-C ACLF score selects patients with high mortality. Combination of static and dynamic scores (CLIF-C ACLF + Lille) improves M28 predictive ability and may be used as futility criteria, in the absence of indication for liver transplant.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0563 THE NON-STEROIDAL FXR AGONISTS PX20606 AND GS-9674 IMPROVE LIVER FIBROSIS AND PORTAL HYPERTENSION IN RODENT MODELS OF CHOLESTATIC, METABOLIC AND TOXIC LIVER CIRRHOSIS

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**Introduction:** FXR agonists show beneficial effects in cholestasis and NASH. We evaluted the non-steroidal FXR agonists PX20606 and GS-9674 in rodent models of toxic (CCl4), and metabolic (NASH) liver fibrosis.

**Aims & Methods:** Toxic model: CCl4 2x/week i.p. for 12weeks. PX20606 (10 mg/kg/day) was given from weeks4–12 of CCl4. NASH model: choline-deficient high-fat diet plus repeated $NaNO_2$ (25 mg/kg i.p., 2x/week) for 10 weeks. GS-9674 (10 mg/kg/day or 30 mg/kg/day) was gavaged from weeks 4–10, with/without propranolol (PROP, 25 mg/kg). At end of treatment, mean arterial pressure (MAP), heart rate (HR), portal pressure (PP) and superior mesenteric artery blood flow (SMABF) were measured. Liver fibrosis was assessed by Sirius Red area (SRA), content of hydroxyproline (HP). Hepatic gene expression was quantified by qRT-PCR.

**Results:** In CCl4 rats, PX treatment ameliorated fibrosis (SRA: 6.99 ± 3.15 vs. 3.97 ± 1.64%; p < 0.001. HP: 415 ± 86 vs. 134 ± 14 μg/g liver;p = 0.002) and decreased AST (555 ± 30 vs. 227 ± 83 IU/ml;p < 0.001) and ALT (538 ± 233 vs. 193 ± 86 IU/ml;p = 0.008). PX decreased PP (11.9 ± 1.4 vs. 9.7 ± 1.4 mmHg;p = 0.037) and increased SMABF (8.88 ± 2.62 vs. 13.81 ± 2.81 ml/min/100 g;p = 0.021), while not affecting MAP or HR. Livers of CCl4–PX rats overexpressed FXR target genes including BSEP (2.5x), SHP (2.3x) and vasodilatory mediators CSH (2.1x) and DDAH (1.7x) while vasoconstrictive endothelin-1 (0.45), PDGF-Rβ (0.51x) and αSMA (0.61x) were reduced. GS-9674 reduced fibrosis in NASH rats in a dose-dependent manner: SRA: VEH:9.62 ± 4.60% vs. GS-9674-10 mg/kg:5.64 ± 4.51% vs. GS-9674-30 mg/kg: 2.94 ± 1.28%;p < 0.001). HP content was reduced by GS-9674-10 mg/kg:6.40 ± 1.33 mg/L and GS-9674-30 mg/kg:6.98 ± 4.74 mg/L vs. NASH-VEH:11.89 ± 2.90 mg/L (p = 0.030). GS-9674-30 mg/kg decreased hepatic col1a1 (-36.5%;p = 0.030) and pdgfr-b (−36.2%;p < 0.001) whereas shp expression was increased (+159%;p < 0.01). GS-9674 decreased PP (11.9 ± 2.1 vs. 8.9 ± 2.2 mmHg;p = 0.020), the combination of GS-9674+PROP reduced SMABF (14.18 ± 3.27 to 10.48 ± 3.74 mL/min/100 g;p = 0.032) while not further decreasing PP.

**Conclusion:** PX20606 ameliorates liver fibrosis and portal pressure in toxic cirrhosis. The novel non-steroidal FXR agonist GS-9674 exerts dose-dependent antifibrotic effects and ameliorates portal hypertension in NASH rats. The addition of propranolol to GS-9674 results in an decrease of mesenteric hyperperfusion.

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C. Kremoser: CEO of Phenex Pharmaceuticals AG
M. Trauner: received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen, and MSD, payments for lectures from Gilead, MSD, and Roche, as well as travel support from Gilead
All other authors have declared no conflicts of interest.

## P0564 THE ROLE OF PNPLA3, RNF7, MERTK AND PCSK7 GENE POLYMORPHISMS IN THE DEVELOPMENT OF LIVER FIBROSIS AND CIRRHOSIS

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**Introduction:** Liver cirrhosis is the end-stage liver diseases, which significantly reduces life quality and expectancy in patients with chronic liver diseases. The most common causes of chronic liver injury include hepatitis C virus (HCV), hepatitis B virus (HBV), alcohol, autoimmune hepatitis and many other conditions. The natural course of liver diseases varies considerably between separate individuals. Some individuals develop liver cirrhosis in a relative short span of year, while in others chronic liver damage does not progress through decades. This inter-individual variability might be related to different confounding factors, including clinical, virulent, environmental, and host factors. Over the last 10 years studies have shown that host genetic factors clearly contribute to the progression of liver fibrosis and development of liver cirrhosis. Genome-wide association studies (GWAS) revealed a link between the risk of developing liver fibrosis (LF) or liver cirrhosis (LC) and single nucleotide polymorphisms (SNPs) of PNPLA3, RNF7, MERTK and PCSK7 genes. PNPLA3 Variations in sequences of the genes encoding PNPLA3, RNF7, MERTK and PCSK7 might be functional and may contribute to the progression of liver injury.

**Aims & Methods:** In this study we aimed to evaluate replicate GWAS results and evaluate associations between PNPLA3 (C > G, rs738409), RNF7 (A > C, rs16851720), MERTK (A > G, rs4374383), and PCSK7 (C > G, rs236918) SNPs and LC or LF. The study included 317 individuals with LC, 154 individuals with LF and 498 healthy controls. The diagnosis and etiology of liver fibrosis and cirrhosis was confirmed by laboratory tests, clinical features, liver biopsy and radiological imaging. Liver fibrosis stage in the biopsy was assessed using METAVIR score. PNPLA3, MERTK, PCSK7 and RNF7 SNPs in all groups were detected using real-time PCR TaqMan® method.

**Results:** Genotypes and alleles of MERTK and PCSK7 SNPs were not associated with the risk of developing LF or LC. RNF7 rs16851720 was associated with LC in recessive model comparing CC vs. AA + CA genotype (aOD: 0.26, CI: 0.09–0.81, p = 0.020). PNPLA3 SNP was linked with higher risk of developing LF (aOD: 1.65, CI: 1.22–2.23, p = 0.001) and LC (aOD: 1.92, CI: 1.49–

2.48, p = 5.57*10–7). PNPLA3 rs738409 was associated with higher risk of developing LF and LC when comparing both dominant (aOD: 1.98, CI: 1.44–2.72, p = 2.20*10–5; aOD: 1.67, CI 1.14–2.43, p = 0.008, respectively) and recessive (aOD: 3.94, CI: 2.03–7.67, p = 5.16*10–5; aOD: 3.02, CI: 1.45–6.28, p = 0.003, respectively) inheritance models.
**Conclusion:** PNPLA3 rs738409 and RNF7 rs16851720 were associated with the risk of developing LF and LC and may contribute to progression to end stage liver disease. MERTK rs4374383and PCSK7 rs236918 SNPs were not linked with the risk of LF and LC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0565 IS THERE THE CONNECTION BETWEEN THE SEROTONERGIC SYSTEM AND CHOLINE ALFOSCERATE IN THE CONDITIONS OF EXPERIMENTAL HEPATIC ENCEPHALOPATHY?

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**Introduction:** Brain serotonin (5-hydroxytryptamine, 5HT) is involved in hypothalamic regulation of energy consumption. That is why it is implicated in the pathogenesis of several metabolic pathologies such as obesity and diabetes mellitus. Several studies have also confirmed its participation in the liver cirrhosis (LC) and hepatic encephalopathy (HE).
**Aims & Methods:** The aim of the study was to establish the state of serotonergic system in the brain and blood in the conditions of LC and concomitant HE in rats and potential impact of standard and novel treatment on the serotonergic system. The study was carried out on four groups of rats: 1st – intact rats and 2nd – $CCl_4$+rats, 3rd – $CCl_4$+standard treatment rats, 4th – $CCl_4$+choline alfoscerate (ChA) rats. Intraperitoneally administration of 1 ml/kg 15% solution of $CCl_4$ in olive oil four times a week for 4 weeks has been done for the modeling of LC and HE in rats. Then the treatment has been performing for one month. The standard administration regimen contained larnamin once daily (75 mg/kg, intraperitoneally (i/p)), rifaximin (10 mg/kg, intragastically (i/g)) and lactulose (1.5 ml/kg, i/g). In the new scheme, animals were treated with lactulose and ChA (15 mg/kg, i/p). In rat brain tissue, 5-HT and tryptophan level, the activity of monoamine oxidases (MAO), tryptophan hydroxylase (TPH), tryptophan decarboxylase (TPDC) and indoleamine-pyrrole 2,3-dioxygenase (IDO) were measured by standard biochemical methods. In rat blood, we estimated the level of 5-HT and tryptophan and the activity of MAO.
**Results:** In the condition of HE, 5-HT in the brain was lower by 60% ($p < 0.05$) as compared with intact, however tryptophan level did not differ. Contrary, in the blood these two parameters were increased by 233% ($p < 0.05$) for 5-HT and 150% ($p < 0.05$) for tryptophan. Standard and novel treatment of HE significantly elevated 5-HT and tryptophan level in the brain and reduced them in the blood. The most pronounced effect was revealed in the 4th group. Thus, ChA increased the level of 5-HT by 101% ($p < 0.05$) and tryptophan by 46% ($p < 0.05$) in the brain and decreased their level by 85% ($p < 0.05$) and 60% ($p < 0.05$) compared with $CCl_4$+rats. It was also found the alteration in the enzymatic activity: the enhancement of MAO in the blood and the fall of the MAO, TPH and IDO activity in the brain, but not the activity of TPDC. The treatment partially restored these parameters to the control values. The ChA had the strongest effect and returned the MAO in the blood to the control benchmark, and increased MAO, TPH and IDO in the brain by 91% ($p < 0.05$), 5.2% ($p < 0.05$) and 4.1% ($p < 0.05$) as for the $CCl_4$+rats.
**Conclusion:** These data suggest the decrease of the 5-HT synthesis in the brain in the conditions of LC and concomitant HE, but its catabolism was not increased because the MAO activity was low and these changes was associated with the elevated level of the 5-HT in the blood. The novel treatment regimen contributed to the normalization of the serotonergic system in the conditions of HE, but the exact molecular mechanisms of such action require unraveling.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0566 REGULATION OF P53 – A POSSIBLE BACTERIAL DEFENSE MECHANISM LEADING TO EPITHELIAL BARRIER DESTABILIZATION IN SPONTANEOUS BACTERIAL PERITONITIS?

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**Introduction:** Spontaneous bacterial peritonitis (SBP) is a life-threatening complication in advancing liver cirrhosis. SBP represents a bacterial infection of ascitic fluid without an intra-abdominal source of infection that could be treated surgically. Translocation of intestinal bacteria or bacterial products from the gut to mesenteric lymph nodes is crucial for SBP, with *Escherichia coli* (*E. coli*), Klebsiella pneumoniae, enterococci and streptococci being the most common germs. As soon as a SBP is suspected, patients must be treated with antibiotics. In this context, biomarkers are in the focus of interest, as they are essential for an initiation of antibiosis on time and a reduced mortality of SBP. However, detection systems or biomarkers for early SBP diagnosis are so far not available.
**Aims & Methods:** With regard to the development of early recognition systems, pathomechanisms and signaling pathways of bacterial translocation in SPB were explored. To investigate effects of intestinal bacteria on epithelial cell junctions, monolayers of human intestinal epithelial cell lines Caco-2 (p53 deficient) and HCT-116 (p53 wildtyp, wt) were cocultured with *E. coli* at day 5 to 8 post confluence. Infection with *E. coli* was performed with a MOI of 10 for 4 hours at each day. Western Blot analysis was performed to analyze changes in intracellular protein levels of Occludin, E-cadherin and the p53 family including p53, p63 and p73.
**Results:** *E. coli* stimulation of HCT-116 cells resulted in a strong decrease of the tight junction protein Occludin, the adherens junction protein E-cadherin, and, remarkably, also p53. Consistently, following *E. coli* stimulation Caco-2 cells displayed reduced protein levels of Occludin and E-cadherin. However, in p53-deficient Caco-2 cells this reduction was less distinct compared to p53-wt HCT-116 cells.
**Conclusion:** These results highlight destabilizing effects of E. coli on intestinal cell junctions. Of specific clinical relevance, a regulation of the tumor suppressor p53 by E. coli was demonstrated. With a more distinctive downregulation in HCT-116 epithelial cells, we hypothesize an involvement of p53 in the regulation of epithelial permeability during bacterial infection. Reduced p53 levels in conjunction with destabilized intestinal epithelial integrity following bacterial infection might represent a mechanism to protect bacteria from intestinal immune responses and therefore to promote bacterial translocation in SBP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0567 IGFBP2–A NOVEL P53-FAMILY TARGET GENE IN HEPATOCELLULAR CARCINOMA

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**Introduction:** p53 transcription factors (p53, p63, p73) respond to cellular stress signals by transcriptional regulation of a specific set of genes. In a number of tumors, also in hepatocellular carcinoma (HCC), p53 family members exert cancerogenic or tumorsuppressive effects. Depending on their splice variants – with transactivation domain (TA) or dominant negative (DN) – p53 proteins activate or inhibit specific target genes. In previous studies we identified the IGFBP2 gene (Insulin-Like Growth Factor Binding Protein 2) as one out of 7 putative target genes for p53 proteins with prognostic relevance in HCC.
**Aims & Methods:** The aim of this study was to characterize the impact of p53 transcription factors on the IGFBP2 gene. Potential p53 family binding sites in the IGFBP2 locus were identified by database analyses (TRANSFAC, JASPAR, TFBIND, PROMO). Hep3B cells were transfected with rAd-p53, -TAp63, -TAp73, -DNp63 or -DNp73 and transcriptional regulation of IFGBP2 was determined by real time qPCR. Intra- and extracellular IGFBP2 protein levels were analyzed by Western Blot and ELISA. Identified putative binding sites were cloned, mutated and evaluated by luciferase reporter assays to confirm p53 family binding.
**Results:** In total, 12 putative p53 family binding sites were identified within the IGFBP2 locus. Intron 1 contains five putative binding sites for p73 and one for p53; another putative p53 binding site is located within the promoter region. TAp73-transfected Hep3B cells displayed a more than 25-fold increased IGFBP2 expression and 10-fold increased intra- and extracellular IGFBP2 protein levels. Transfection with TAp53 resulted in an up to 7-fold increased IGFBP2 expression. Intron1-dependent luciferase activity was increased by up to 150-fold in TAp73-transfected cells. Moreover, luciferase assays confirmed the identified p53 binding site in intron 1, since luciferase activity (initially induced by up to 20-fold in TAp53 transfected cells) was reduced by up to 90% after mutation and deletion, respectively, of the putative p53 binding sequence.
**Conclusion:** These results identify IGFBP2 as novel target gene for TAp73 and TAp53 in HCC. We demonstrate for the first time, that TAp73 interacts with IGFBP2 signaling, underlining the important link between p53 and IGF pathways. In this context, the p53 family network acts as tumor-inhibiting mechanism, whereas the axis of IGF growth factors is a crucial mediator of cell proliferation. It is suggestive, that the particular balance of these two signaling pathways decides on growth, cancerogenesis and treatment response. Thus, fine-tuning of these pathways might be capable of adjusting a cell's resistance to chemotherapeutic drugs and offers new therapeutic options.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0568 QUINOLINIC ACID AS A PREDICTOR OF OUTCOME IN CIRRHOTIC PATIENTS

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**Background:** Liver cirrhosis and its complications are major health problem (1). Number of predictors of prognosis of liver cirrhosis was established. The most widely used and applicable ones are Child (2) and MELD (3) scores. There are some deficiencies concerning both of them. Quinolinic acid (QuinA) is a product of the kynurenine pathway, it acts as a neurotoxin, gliotoxin, pro-inflammatory mediator and pro-oxidant molecule(4).
**Aim:** To assess the role of QuinA as a predictor of outcome in patients with liver cirrhosis.
**Patients and methods:** The study included 80 patients with liver cirrhosis and 10 healthy persons as controls. Child-Pugh and MELD scores were calculated. All patients were subjected to complete history taking, full clinical examination, pelvi-abdominal ultrasonography, laboratory investigations; complete blood picture, liver and kidney profiles, coagulation profile, random blood glucose level and serum QuinA by ELISA. Six months follow-up were done for all patients

according to clinical, routine laboratory parameters and ultra sound examination with assessment of mortality
**Results:** After 6 months with assessment of mortality, 20 patients died. There was positive significant correlation between baseline QuinA values and baseline Child and MELD scores. Regarding prediction of complications after 6 months, both Child and MELD scores showed sensitivity more than that of QuinA levels, while QuinA levels showed higher specificity. QuinA values were the most sensitive and specific for prediction of mortality after 6 months when compared to Child and MELD scores.
**Conclusion:** Serum levels of QuinA increased markedly according to progressive liver dysfunction and correlated to high values of Child and MELD scores. QuinA was a specific marker for complications in cirrhotic patients particularly hepatic encephalopathy, while it was an excellent marker for prediction of mortality in those patients. It means that it is a good prognostic marker for prediction of outcome in cirrhotic patients, however its low sensitivity in prediction of complications reduce its value in screening of these complications
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0569 VITAMIN D DEFICIENCY IN LIVER CIRRHOSIS


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**Introduction:** The presence of vitamin D deficiency (VDD) is now widely recognized to be associated with many systemic disorders, such as chronic liver diseases (1). However, its association with alcoholic liver disease (ALD) has been poorly described.
**Aims & Methods:** The aim of this study was to compare the prevalence of vitamin D deficiency in patients with alcoholic cirrhosis and hepatitis C cirrhosis. We performed a prospective study, conducted over a period of 12 months (October 20114–September 2015). The study enrolled 84 patients diagnosed with liver cirrhosis (42 with hepatitis C cirrhosis and 42 with alcoholic cirrhosis). Serum 25(OH) D levels were measured in all patients enrolled in the study. Severity of vitamin D deficiency was graded as mild (20–30 ng/ml), moderate (7–19 ng/ml) or severe (<7 ng/ml), normal being >30 ng/ml.
**Results:** Of patients, 84% presented some degree of vitamin D deficiency. In the hepatitis C cirrhosis group, 18% had mild, 46% had moderate, and 36% had severe vitamin D deficiency. In the alcoholic cirrhosis group, 22% had mild, 41% had moderate, and 37% had severe vitamin D deficiency. There was no statistical difference between groups regarding vitamin D deficiency (41% vs. 43%). Female gender were independent predictors of severe vitamin D deficiency in chronic liver disease.
**Conclusion:** Chronic liver disease patients are at very high risk of vitamin D deficiency regardless of etiology or severity. This patients have an increased risk for the development of osteoporosis and fractures, reduced muscle strength, an impaired inflammatory response, and malignancy (2). Females are at highest risk of vitamin D deficiency.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0570 IMPROVEMENT OF THE MODELING AND DIAGNOSIS OF HEPATIC ENCEPHALOPATHY IN RATS


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**Introduction:** Modeling of liver cirrhosis (LC) and hepatic encephalopathy (HE) in rats has some limitations namely high mortality of lab animals or high duration of LC formation. Diagnosis of HE was accomplished with the model of food conditioned reflex that allowed to evaluate only locomotor activity of animals but not their ability to think and remember.
**Aims & Methods:** The aim of the study was the optimization of the HE modeling and diagnosis. Intraperitoneal administration of 1 ml/kg 15% solution of $CCl_4$ in olive oil four times a week for 4 weeks has been suggested for optimal simulation of HE in rats. The development of HE, namely the ability of animals to memorization, learning and thinking was studied by the formation of a food conditioned reflex in the T-shaped maze. 14 rats were divided into two groups: 1st – intact rats and 2nd – rats pretreated with $CCl_4$. The dynamic of reducing the time of getting animals to the food reinforcement in the maze as a result of remembering the location of food was estimated during 14 days.
**Results:** In the first day of food conditioned reflex study it was established that intact rats reached the food in $157 \pm 47$ sec. Contrary, the time of getting to food of $CCl_4$-rats was 2,1 times ($p < 0.05$) longer that suggests the less activity and lethargy of these animals. In the next 7 days, there were not any changes in the time of getting to food in T-shape maze in the intact group as well as in the group pretreated with $CCl_4$. Since the 7th day we have shown a steady acceleration of finding the food by intact rats. However, there were not registered data about faster food reinforcement in the group of animals that got $CCl_4$ injection. Moreover, in the group of intact rats we have established the decrease in time of finding the food by 92% ($p < 0.05$) as compared with the first day of experiment. Such changes were not obvious for the $CCl_4$-group: we did not find the significant difference between the reaching food of $CCl_4$-rats at the start and at the 14th day of experiment in the T-shaped maze. Thus, we registered that the time of finding the food in the $CCl_4$ group was 21.4 ($p < 0.001$) greater than in the intact group at the 14th day of study in the T-shaped maze. The impairment of food conditioned reflex formation has showed lack of remembering and thinking in rats pretreated with $CCl_4$.
**Conclusion:** We have updated the scheme of modeling LC and HE by the decrease of time of the LC development and the reduction of animal mortality as result of toxic action by $CCl_4$. The improved diagnosis of HE was achieved by using the methodology of forming a food conditioned reflex in rats. This method can be recommended as a basic for HE modeling and can be used for study new treatment strategies of this disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0571 PROGNOSIS OF PATIENTS WITH ESOPHAGEAL VARICES POST BANDING ULCER BLEEDING


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**Introduction:** Bleeding from post-endoscopic band ligation (EBL) ulcer is associated with a high mortality, for which outcome and prognostic indicators are unknown.
**Aims & Methods: Aims:** to identify predictors of poor outcome for variceal post-EBL ulcer bleeding and its impact in short and long term mortality; to compare mortality among patients with bleedind from post-EBL ulcer and from esophageal variceal rupture (EVR).
**Methods:** Case control study. Cases: all admissions for post-EBL ulcer bleeding, in a tertiary gastrointestinal service, from January 2003 to December 2015. Controls: EBL treated patients due to acute esophageal variceal hemorrhage. Endpoints: mortality assessed at 7, 28, 90, 180 and 360 days post-therapeutic.
**Results:** A total of 50 post-EBL ulcer bleeding cases were included. Mean age ($57.1 \pm 12.0$); male:female ratio (4.1:1). Cirrhosis etiologies: alcoholic (70.7%), HCV (29.3%) and HBV (15.7%). Child-Pugh-Turcotte (CPT) distribution: A (17.3%), B (46%) and C (36.7%); mean MELD was $14.5 \pm 6.1$. Hepatocellular carcinoma and thrombosis of the portal vein were present in 14% and 24%, respectively. Treatment: endoscopic therapy in 34%, balloon tamponade in 20% and TIPS placing in 8%. Rebleeding in 22% and failure to control hemorrhage in 1 case. Mortality at 7, 28, 180 and 360 days was 2%, 14%, 30% and 34%, respectively, showing no difference from control group (p = n.s). Presence of hepatorenal syndrome (HRS) was associated with mortality at 28 (OR:30 $p < 0.001$), 180 (OR:8 $p = 0.049$) and 360 days (OR:8, $p = 0.005$), while alcoholic cirrhosis and spontaneous bacterial peritonitis (SBP) were associated with mortality at 180 and 360 days. In multivariate analysis, only the HSR (28, 180 and 360 days) and SBP (360 days) were independent risk factors for mortality.
**Conclusion:** Mortality due to post-EBL ulcer bleeding was high, and was not attributable to bleeding-treatment failure. The presence of hepatorenal syndrome and spontaneous bacterial peritonitis were independently associated with poor outcome, regardless of CPT classe.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0572 DOES NON-INVASIVE ASPARTATE AMINOTRANSFERASE/ PLATELET RATIO INDEX (APRI) CORRELATES WITH INVASIVE HEPATIC VENOUS PRESSURE GRADIENT (HVPG) IN CIRRHOSIS?

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**Introduction:** Hepatic Venous Pressure Gradient (HVPG) is the only recommended tool to measure portal hypertension and prognosticate complications of cirrhosis. Aminotransferase/platelet ratio index (APRI) is simple noninvasive marker of hepatic fibrosis.

**Aim:** To compare non-invasive APRI score with invasive HVPG for portal hypertension and determine the usefulness of APRI in predicting complication of portal hypertension

**Methods:** APRI and HVPG were measured in consecutive patients of cirrhosis aged 18 to 70 years in the year 2011–2014 admitted to our department.

**Results:** Study included 277 patients with median age 51years (48–63years); 228 (82.31%) males. Etiology of cirrhosis were alcohol 135(48.7%), Viral (12.3%), Cryptogenic/NAFLD 78(28.2%) and others 30(10.8%). Mean CTP score and mean MELD score were $7.33 \pm 1.7$ and $16.85 \pm 6.4$ respectively. Median HVPG was $16.69 \pm 5.43$ mmHg. Maximum Youden's index was 0.479 which corresponded to a cut-off value of 0.876 of APRI. The ROC curve to study the performance of APRI for predicting portal pressure (HVPG $>12$ mmHg) had area under curve 0.753 ($P < 0.001$). APRI of 0.876 had a sensitivity 69.5%, specificity 78.4%, diagnostic accuracy 71.12% and positive predictive value 93.45% for predicting HVPG $>12$ mmHg. There was significant difference (Spearman's Rho = 0.443; $p < 0.001$) in median APRI of patient with HVPG $\leq 12$ mmHg (APRI- 0.66) and those with HVPG $>12$ mmHg (APRI-1.40) respectively. Median APRI in upper GI bleed patient was 1.441 which was significantly higher than non bleeder patient APRI- 0.985($p < 0.001$).

**Conclusion:** APRI score of 0.876 seems to have an acceptable accuracy for prediction of high portal pressure. High APRI will predict more bleeding complications. APRI is a simple, non invasive and cost-effective parameter for diagnosis of high portal pressure in patients with cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0573 SERUM LEVELS OF LECTIN COMPLEMENT PATHWAY MOLECULES DO NOT PRIMARILY DETERMINE THE RISK OF BACTERIAL INFECTIONS IN PATIENTS WITH CIRRHOSIS

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**Introduction:** Bacterial infections are a significant cause of morbidity and mortality in cirrhosis. Lectin pathway molecules of the complement system are synthesized in the liver and have a pivotal role in the innate host defense against infectious organisms. Mannose-binding lectin (MBL) and ficolins (FCNs) act as soluble pattern recognition molecules, while mannan-binding lectin serine proteases (MASPs) do as effector molecules in elimination of the pathogens. Low levels of the functional proteins increase the risk of various infectious diseases mostly in immune-deficient conditions but their significance has scarcely been investigated in cirrhosis related bacterial infections.

**Aims & Methods:** Sera of 266 patients with cirrhosis (male: 50%, alcoholics: 63.9%, median age: 56 years and MELD score: 11), and 160 healthy subjects were assayed for the concentrations of a panel of lectin molecules (FCN-2, FCN-3 and MASP-2) by sandwich-type immunoassay. In cirrhosis, a 5-year follow-up observational study was conducted to assess a possible association between lectin levels and development of clinically significant bacterial infections (CSI) and mortality.

**Results:** The FCN-2, FCN-3 and MASP-2 levels were significantly lower in cirrhosis compared to healthy controls (median, 505 vs. 769 ng/ml, 7301 vs. 10797 ng/ml and 212 vs. 412 ng/ml, respectively, $p < 0.001$ for all) and decreased according to disease severity as rated by Child-Pugh stage. In Kaplan-Meier analysis with LogRank test, time to development of CSI was associated with low level of FCN-3 (<4857 ng/ml, $p = 0.028$) but not FCN-2 (<427 ng/ml, $p = 0.068$) or MASP-2 deficiency ($p = 0.368$). Combined FCN deficiency even more than individual molecules were able to predict the development of these episodes. Patients with low level of both FCNs had a cumulative risk of an infection of 52% as compared to 31% with normal level of FCNs ($p = 0.021$). None of the lectin molecules, however, were associated to long-term mortality. In multivariate Cox-regression analysis, clinical factors but not the serum lectin profile remained an independent predictor of CSI. Prior episode of CSI and in a stepwise manner, the disease severity as rated by Child-Pugh stage conferred higher risk for development of CSI (HR: 2.64, 95% CI: 1.74–3.99, $p < 0.001$ and 2.11, 95%CI: 1.52–2.93, $p < 0.001$, respectively).

**Conclusion:** In the present prospective study, diseases severity and prior episode of CSI but not the serum lectin profile were major determinants of the risk of CSI in cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0574 SAFETY OF DAA THERAPY REGARDING RENAL FUNCTION IN POST-LIVER TRANSPLANT PATIENTS INFECTED WITH HEPATITIS C INDEPENDENT OF PRE-EXISTING RENAL IMPAIRMENT, AND A 100% SVR12 RATE – A SINGLE-CENTRE STUDY

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**Introduction:** Direct acting antiviral (DAA) therapy of hepatitis c virus (HCV) infection is yet well established in patients with and without cirrhosis of the liver. In times of low efficiency and Interferon treatment liver transplantation has frequently been necessary in patients with chronic HCV infection, especially for those with advanced cirrhosis or HCC. Patients after liver transplantation with ongoing HCV infection often suffer from renal and hepatic impairment. A major concern when treating HCV patients after liver transplantation is the potential interaction of DAA and immunosuppressive therapy that might result in decreasing renal function.

**Aims & Methods:** In this single-centre study we analysed clinical parameters of 18 HCV infected patients treated with DAA therapy after liver transplantation. The primary endpoints were change of renal function (GFR and creatinine levels) and viral eradication 12 weeks after therapy (SVR 12). For secondary endpoints we investigated the influence of DAA therapy over the time on following parameters: transaminases, bilirubin, INR, ARFI measurement and MELD Score. Subgroup analyses were performed for renal impairment, the type of immunosuppressant and the type of DAA Regime.

**Results:** Form the 18 patients treated 5 suffered of renal impairment grade 2, and 7 patients of renal impairment grade 3. The remaining 6 patients had no/mild renal impairment. No patient was on haemodialysis. Renal function at SVR 12 was neither influenced by the type of immunosuppressant nor the type of DAA regime, nor whether there was pre-existing renal impairment. All patients reached SVR12, regardless of the genotype (4 patients genotype 3; 14 patients genotype 1) or the type of DAA regime (9 patients Daclatasvir and Sofosbuvir / 2 patients additionally ribavirin; 9 patients Ledipasvir, Sofosbuvir / 8 patients additionally ribavirin). In respect of secondary endpoints the type of immunosuppressant had no influence on renal function or SVR12 rate. The levels of transaminases and bilirubin declined as expected. 10 patients had already liver fibrosis greater than F3 in non-invasive measurement before initiation of treatment. Even in this short period of time single point acoustic radiation force impulse imaging (ARFI) improved in 9 patients ($p = 0.012$) and albumin levels tended to increase under therapy ($p = 0.055$). In 7 patients MELD score improved, due to the decrease of bilirubin levels.

**Conclusion:** Over all, DAA-therapy in liver transplant patients was effective and save in this single-centre real-life cohort. Renal function was not influenced by the administered drug combinations, even in patients with pre-existing renal impairment. No safety issues occurred.

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All other authors have declared no conflicts of interest.

## P0575 CONCOMITANT NSBB TREATMENT DOES NOT INCREASE EFFICACY OF EBL IN PRIMARY PROPHYLAXIS BUT IMPROVES SURVIVAL IN SECONDARY PROPHYLAXIS OF VARICEAL BLEEDING

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**Introduction:** Endoscopic band ligation (EBL) is used for primary (PP) and for secondary prophylaxis (SP) of variceal bleeding in cirrhotic patients with gastro-esophageal varices (GEVs). While the addition of non-selective beta-blockers (NSBBs) to EBL is recommended for SP, in PP either EBL or NSBB should be used.
**Aims & Methods:** Retrospective assessment of the efficacy of EBL for PP and SP of variceal bleeding in two tertiary care centers in Vienna. Rebleeding rates and transplant-free survival were assessed with and without concomitant NSBB therapy.
**Results:** 766 patients with GEVs were treated with EBL. Among the 284 patients undergoing sequential EBL for PP, n = 95 (33.5%) received EBL only while n = 187 (65.8%) received concomitant EBL+NSBBs. Among the n = 482 patients on SP, n = 163 (33.8%) received EBL only while n = 306 (63.5%) received EBL/NSBB combination therapy.
In PP, concomitant NSBB therapy did neither decrease bleeding rate (9.0% vs. 10.3% at Y1, 16.2% vs. 13.5% at Y2, 19.3% vs. 14.9% at Y3, log-rank p = 0.747) nor mortality (29.6% vs. 19.2% at Y1, 39.7% vs. 31.8% at Y2, 45.9% vs. 38.3% at Y3, log-rank p = 0.389) as compared to EBL alone. In SP, the combination of EBL/NSBB did not decrease bleeding rates as compared to EBL alone (25.1% vs. 23.7% at Y1, 27.8% vs. 30.4% at Y2, 32.5% vs. 33.8% at Y3, log-rank p = 0.822) but was associated with a significantly lower mortality rate (17.1% vs. 46.2% at Y1, 22.5% vs. 48.7% at Y2, 31.8% vs. 49.7% at Y3, log-rank $p < 0.001$).
**Conclusion:** EBL alone is as sufficient as EBL/NSBB combination for primary prophylaxis of variceal bleeding. In absence of contraindications to NSBB, the EBL should always be combined with NSBB in secondary propylaxis of variceal bleeding, since it improves survival as compared to EBL alone.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0576 RE-BLEEDING RATES AND SURVIVAL AFTER EARLY TIPS IN CLINICAL PRACTICE

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**Introduction:** Early implantation of a transjugular intrahepatic portosystemic shunt (TIPS) has been shown to improve survival after acute variceal bleeding (AVB) in highly selected patients. However, data on real-life cohorts is scarce.
**Aims & Methods:** To identify and evaluate outcome of adult patients with cirrhosis undergoing early TIPS implantation within 72 hours after AVB at two tertiary care centers in Vienna from 1994–2014.
**Results:** Forty-nine patients with early TIPS after AVB were included. Mean MELD score was: 14.4±4.4. Thirteen patients (26.5%) presented characteristics that were exclusion criteria in previous early TIPS trials ('stringent criteria': n = 3 age > 75, n = 3 CPS > 13, n = 1 HCC > Milan, n = 5 previous beta-blocker/band-ligation, n = 1 renal insufficiency). Bare metal and PTFE-covered stents were used in 32 (65.3%) and 17 (34.7%) patients, respectively. Early rebleeding (< 6weeks) occurred in 8.2% (4/49) patients and 6-weeks bleeding-related mortality was 28.6% (12/49). Bare and PTFE-TIPS patients showed similar early rebleeding rates (9.9% vs. 6.3%, p = 0.627) and bleeding-related mortality (22.6% vs. 11.8%, p = 0.389). Overall rebleeding rate was lower in PTFE-TIPS patients (61.5% vs. 6.3%, p = 0.002; median follow-up of 18.5 months). Survival tended to be longer in patients receiving PTFE-TIPS vs. bare stents (median 21.5 vs. 9.6 months, p = 0.212). Survival was significantly better in patients meeting stringent early TIPS criteria ($p < 0.001$), especially in those with PTFE-TIPS (58.1 vs. 10.7 months in bare stents, p = 0.029).
**Conclusion:** An early TIPS strategy controls acute variceal bleeding in most cases. The use of early PTFE-TIPS for acute variceal bleeding results in a favorable outcome in a real-life cohort of cirrhotic patients fulfilling 'stringent' selection criteria.
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All other authors have declared no conflicts of interest.

## P0577 ACUTE-ON-CHRONIC LIVER FAILURE AN UNDENIABLE ENTITY

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**Introduction:** The last 5–7 years in hepatology saw the genesis of a new clinical nosologic entity called Acute-on-chronic liver failure (ACLF). Following the initial theoric idea formal objective criteria were defined based and supported by good quality clinical studies such as CANONIC (Moreau R & Consortium., 2013) that produced strong evidence to justify this new concept. However, the clinical relevance and true independence of this entity has been frequently questioned and challenged.
**Aims & Methods:** The objective was to identify and characterize this clinical condition in a Gastroenterology department including its associated intensive care unit. We performed a single-center prospective study (during 18 months) with inclusion of every patient admitted with acute decompensation of chronic liver disease (CLD). Exclusion criteria considered were: any stage of hepatocellular carcinoma, acute or chronic extra-hepatic severe medical condition that might have contributed to the acute decompensation particularly chronic kidney disease, chronic decompensated heart failure, any oncologic condition and trauma. Exclusion of the patients without, at least, 3 months of follow-up. Identification of the patients with ACLF according to the criteria defined by the study CANONIC. ACLF was graded also with those criteria. Statistics done with SPSS v. 20 (SPSS Inc. v. 20, IBM, Chicago IL).
**Results:** 118 patients enrolled at their first admission in the period of the study (July 2014 – December 2015). The majority were men (76.3%). Mean age of 60.0 ± 11.2 years (36 to 84). The most common etiologies of the CLD were alcohol consumption (81.4%), HCV + alcohol (5.9%), HBV + HCV + alcohol (2.5%) and primary biliary cholangitis (2.5%). There were 39 patients admitted with ACLF (33.1%), the majority with ACLF – grade 1 (61.5%). In the univariate analysis the presence of ascites – odds ratio 3.64 (95% CI 1.66–8.0), infection (spontaneous bacterial peritonitis or sepsis with other cause) odds ratio 4.38 (95% CI 2.36–8.12) and hepatorenal syndrome – odds ratio 4.66 (95% CI 3.11–6.97) all correlated with higher risk of ACLF but the presence of acute upper digestive bleeding (mainly by variceal bleeding) had a negative correlation for ACLF – odds ratio 0.49 (95% CI 0.28–0.88) ($p < 0.05$). In the multivariate analysis the presence of infection or hepatorenal syndrome showed

higher risk for ACLF development ($p < 0.0001$ and $p = 0.002$ respectively). The ACLF group had higher short-term (28-day) and 3 month mortality, respectively 43.6% and 64.1% comparing to the no-ACLF group: 2.5% and 7.6% ($p < 0.0001$).
**Conclusion:** the presence of ACLF is linked to a considerable higher risk of short-term mortality in the patient with CLD. Sepsis and acute kidney injury occur frequently in this condition and can be often present in a subtle/attenuated way so they must be carefully searched and efficiently treated. On the opposite side, in this study, an important clinical event like acute variceal bleeding correlated with lower risk for development of ACLF.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0578 ERECTIL (DYS) FUNCTION IN PATIENTS WITH LIVER CIRRHOSIS: A CROSS-SECTIONAL STUDY

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**Introduction:** Previous studies have evaluated erectile dysfunction (ED) in patients with chronic liver disease (CLD). However, the association between ED and other complications of liver cirrhosis (LC) has not been widely studied [1].
**Aims & Methods:** The aim of this study was to evaluate the independent risk factors for ED in patients with CLD. This is a cross-sectional study in subjects with CLD in which a simplified version the International Index of Erectile Function questionnaire was applied. Exclusion criteria were as follows: age $>75$ years old and alcohol intake $>40$ g/day. Statistics analysis were performed using IBM SPSS Statistics 22 with $p < 0.05$ deemed to be statistically significant.
**Results:** We included 66 male patients with CLD, median age was 55.5 years (IQR: 47.5–62.0), and 77% were married. Forty three percent of the patients evaluated had liver cirrhosis (LC), mainly Child-Pugh A (64.3%), being alcohol the most frequent etiology (25.8%). Globally, 62.1% of the patients fulfilled criteria for ED, 10.6% characterized as severe ED, and among patients with LC the diagnosis of ED was made in 82% of them. Twenty percent of patients surveyed confirmed that had previously taken drugs not prescribed by a doctor to increase their sexual performance. The presence of ED was associated with LC ($p = 0.006$), severity of LC ($p = 0.014$), presence of esophageal varices ($p < 0.001$), refractory ascites ($p = 0.006$), previous hospitalization due to decompensated cirrhosis ($p = 0.006$), use of diuretics ($p = 0.041$) and smoking habits ($p = 0.003$). In our study, there was no association between the presence of ED and previous episodes of hepatic encephalopathy, presence of diabetes mellitus, dyslipidaemia, hypertension or use of beta-blockers. In a linear regression model that included the following factors: age, smoking habits, previous decompensation, presence of LC and Child-Pugh score, only the latter two variables were independent factors for the presence of ED. The presence of LC was associated with an OR = 5.11 (95% IC: 1.06–16.27) for the diagnosis of ED.
**Conclusion:** The presence of LC, specially in more advanced stages, was an independent risk factor for the presence of ED, apart from other classic factors, such as: smoking habits and diabetes mellitus.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0579 ELECTROCARDIOGRAPHIC CHANGES IN LIVER CIRRHOSIS

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**Introduction:** Cirrhotic cardiomyopathy, manifested as an impaired contractile response to stressful stimuli, damaged diastolic relaxation and electrophysiological abnormalities, is a chronic cardiac dysfuntion in patients with liver cirrhosis. Prolonged QT interval represents the most important electrocardiographic (ECG) finding in these patients, being a risk factor for ventricular arrhythmias.
**Aims & Methods:** The aim of this study was to find correlations between ECG changes in cirrhotic patients and prognostic scores for disease severity, and analyze the relationship between the use of non-selective beta blockers (NSBBs) and QTc interval prolongation. This retrospective study conducted in the Clinic of Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, included 251 patients with liver cirrhosis, who were consecutively hospitalized in the period from 2013–2015. According to etiology of cirrhosis, the patients were divided into two groups: alcoholic and non-alcoholic. Based on laboratory values and clinical findings, prognostic scores including Model for End-Stage Liver Disease (MELD) and Child-Pugh were calculated, along with a 12-lead ECG in each patient on the day of admission. Heart rate (HR), PQ interval, QT interval, QRS duration, and voltage of QRS complexes in precordial and limb leads were analyzed.
**Results:** Alcoholic liver cirrhosis was diagnosed in 109 (43.43%) and non-alcoholic in 142 (56.57%) patients. There was a statistically significant positive correlation between QTc and MELD and Child-Pugh scores and a negative correlation between the voltage of the QRS complex in the limb leads and the prognostic scores. The average length of QTc in the alcoholic group was $434.16 \pm 42.82$ ms and $410.76 \pm 52.56$ ms in the non-alcoholic group ($p < 0.001$) (Table 1). There were no statistically significant correlations between PQ interval and QRS complexes with MELD and Child-Pugh scores in both observed groups. Similarly, there were no statistically significant differences in QTc prolongation between patients who had and had not received NSBBs (QTc $= 415.17 \pm 56.44$ vs $426.91 \pm 41.40$) ($p = 0.066$).

**Table 1:** Mean values of parameters based on etiology of cirrhosis ($n = 251$)

| Parameter | Alcoholic Cirrhosis | Non-alcoholic Cirrhosis | P-value |
|---|---|---|---|
| MELD | $14.26 \pm 7.02$ | $12.49 \pm 6.64$ | 0.075 |
| HR | $80.14 \pm 20.85$ | $74.83 \pm 15.69$ | 0.023* |
| PQ (ms) | $150.07 \pm 37.97$ | $149.98 \pm 35.82$ | 0.975 |
| QTc | $434.16 \pm 42.82$ | $410.76 \pm 52.56$ | <0.001* |
| QRS (ms) | $92.85 \pm 32.68$ | $91.33 \pm 39.85$ | 0.745 |
| QRS Voltage (precordial leads) | $14.56 \pm 5.60$ | $14.71 \pm 6.56$ | 0.849 |
| QRS voltage (limb leads) | $6.56 \pm 2.81$ | $8.12 \pm 3.30$ | <0.001* |

* Statistically significant, MELD: Model for End-Stage Liver Disease Score, HR: heart rate, OTc: corrected QT for the heart rate.

**Conclusion:** These findings imply that patients with liver cirrhosis have prolonged OTc interval, as a consequence of abnormal ventricular repolarization, and this prolongation is greater in those with alcoholic liver cirrhosis. Voltage of QRS complex in limb leads is lower in patients with advanced liver cirrhosis because of peripheral oedema. Patients who are on NSBBs for portal hypertension do not have an increased risk for ventricular arrhythmias including torsades de pointes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0580 PROPRANOLOL AND LOSARTAN ADMINISTRATION IN PATIENTS WITH DIFFERENT STAGES OF LIVER CIRRHOSIS

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**Introduction:** Nonselective beta-blockers and angiotensin II receptor antagonists are widely used in the pharmacological treatment of portal hypertension. In the last years was reported about antifibrotic effect of angiotensin II receptor antagonists in chronic liver diseases.

**Aims & Methods:** Our study included 115 patients with liver cirrhosis in different stages. 27 patients with compensated liver cirrhosis (Child-Pugh class A) and 28 patients with decompensated cirrhosis (Child-Pugh class B and C) received Losartan 25 mg/day. 29 patients with compensated liver cirrhosis and 31 patients with decompensated cirrhosis received Propranolol 30 – 120 mg/day. Initially and after 6 months of treatment using color duplex Doppler ultrasonography we appreciated portal vein and splenic vein diameter, portal blood flow, portal blood flow velocity and hepatic artery resistance index.

**Results:** After 6 months of treatment we found different changes in different groups of study. Propranolol administration in decompensated liver cirrhosis versus compensated cirrhosis significantly decreased portal blood flow ($17.7 \pm 0.9\%$ vs $12.1 \pm 0.6\%$, $p < 0.05$), portal vein diameter ($16.8 \pm 0.7\%$ vs $11.8 \pm 0.7\%$, $p < 0.05$) and splenic vein diameter ($15.3 \pm 0.5\%$ vs $10.8 \pm 0.7\%$, $p < 0.05$). Portal blood flow velocity and hepatic artery resistance index changed significantly after 6 months of treatment in Propranolol administration groups, but no significant differences were found between these groups ($p > 0.05$). Losartan administration significantly increased portal blood flow velocity in compensated liver cirrhosis versus decompensated cirrhosis ($15.5 \pm 0.8\%$ vs $10.8 \pm 0.7\%$, $p < 0.05$) and significantly decreased hepatic artery resistance index in compensated liver cirrhosis compared with decompensated cirrhosis ($16.8 \pm 0.9\%$ vs $11.2 \pm 0.8\%$, $p < 0.05$). Portal vein and splenic vein diameter, portal blood flow changed significantly after 6 months of treatment in Losartan administration groups, but no significant differences were found between both study groups ($p > 0.05$).

**Conclusion:** Our study indicated that the target of Propranolol administration is portal blood flow that is more increased in decompensated cirrhosis. The main target of Losartan administration is intrahepatic resistance that can be better remodeled in compensated cirrhosis than in advanced liver cirrhosis. Intrahepatic resistance decreases, probably, by antifibrotic effect of Losartan, which is expressed in compensated cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0581 ULTRASOUND-BASED ELASTOGRAPHIC METHODS FOR THE PREDICTION OF ESOPHAGEAL VARICES IN LIVER CIRRHOSIS

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**Introduction:** Ultrasound-based elastographic methods are non-invasive techniques for the evaluation of liver stiffness (LS) that might be also useful in the assessment of portal hypertension.

**Aims & Methods:** The aim of this study was to evaluate the performance of 4 ultrasound based elastographic methods for predicting the presence of esophageal varices (EV) in patients known with liver cirrhosis.

**Material and method**: the study included 130 consecutive subjects diagnosed with liver cirrhosis (with clinical, biological, ultrasound, endoscopical or histological signs of liver cirrhosis), in whom LS was evaluated in the same session by means of 4 elastographic methods: transient elastography (TE) (M and XL probes) (FibroScan, EchoSens), ARFI (VTQ) (Acuson S2000, Siemens), 2D-SWE [Aixplorer, Supersonic Imagining (SSI)] and 2D-SWE. GE (LOGIQ E9, General Electrics Healthcare). Reliable LS measurements were defined as: for TE, VTQ and 2D-SWE. GE-the median value of 10 measurements and for 2D-SWE the median value of 3 measurements acquired in a homogenous area. In 75 patients out of 130 all 4 elastographic methods had valid measurements and were included in the final analysis.

**Results:** 29/75 patients from the study group had EV while 46/75 had not. The mean LS values for patients without EV were lower as compared to those of patients with EV: TE ($23.02 \pm 9.67$ KPa vs. $28.01 \pm 12.81$ KPa, $p = 0.05$), 2D-SWE($20.18 \pm 11.75$ KPa vs. $23.32 \pm 14.45$ KPa, $p = 0.29$), ARFI ($2.50 \pm 0.67$ m/s vs. $2.67 \pm 0.70$ m/s, $p = 0.28$), 2D-SWE. GE ($10.69 \pm 6.52$ KPa vs. $11.47 \pm 6.46$ KPa, $p = 0.60$). TE had the best performance for predicting EV. The following cut-off were establish for predicting the EV (table):

| Elastographic technique cut off | Se | Sp | NPV | PPV | AUROC | |
|---|---|---|---|---|---|---|
| **TE** $\geq$21.1 kPa | 80.8% | 50% | 82.8% | 46.7% | 0.68 | $p = 0.04$ |
| **ARFI(VTQ):** $>3.08$ m/s | 37% | 83.3% | 70.2% | 55.6% | 0.58 | $p = 0.25$ |
| **2D-SWE:** $>13.2$ kPa | 96.3% | 25% | 92.3% | 41.9% | 0.60 | $p = 0.12$ |
| **2D-SWE. GE:** $>13.3$ kPa | 74.7% | 58.3% | 80% | 50% | 0.65 | $p = 0.02$ |

**Conclusion**: LS values assessed by any ultrasound based elastographic methods are higher in patients with EV as compared to those without EV, but TE seems to be the most predictive for the presence of EV.

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## P0582 PLATELET COUNT TO PORTAL VEIN DIAMETER RATIO AS A NOVEL PREDICTOR OF ESOPHAGEAL VARICE IN PATIENTS WITH LIVER CIRRHOSIS

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**Introduction:** Patients with liver cirrhosis predispose to several complications with large burden of morbidity and mortality. One of the most fearful complications of liver cirrhosis is development of esophageal varices and subsequent variceal bleeding with considerable mortality. Upper endoscopy is now considered the gold standard modality for diagnosis of esophageal varices. Due to large burden of esophageal varices in cirrhosis, both their early and non invasive detection have been increasingly considered in different studies.

**Aims & Methods:** This study aimed to investigate use of platelet count to portal vein diameter ratio for detection of esophageal varices in patients with liver cirrhosis. Adult patients (>18 years) diagnosed with liver cirrhosis of different etiologies who were referred to Shiraz transplant center for liver transplantation between October 2012 and October 2015 were included in the study. All of these patients have undergone upper endoscopy for screening of esophageal and gastric varices. Color Doppler sonography of abdominal vessels and contrast enhanced abdominal computed tomography (CT) were also performed as routine pre-transplant check up for all cirrhotic patients awaiting liver transplantation. Patients 'characteristics including sex, age, underlying cause of cirrhosis as well as liver function test, coagulation profile, model for end stage liver disease (MELD) score, cell blood count, platelet cunt, size of spleen and diameter of portal vein were recorded using a data gathering form. Patients with isolated gastric varices and those with simultaneous gastric and esophageal varices were excluded.

**Results:** From 989 patients with liver cirrhosis, 524 patients (52.9%) found to have esophageal varices in upper endoscopy. Grade 1, 2 and 3 esophageal varices were found in 183, 198 and 143 patients respectively. In univariate analysis, platelet count, aspartate aminotransferase (AST), total bilirubin and alkaline phosphatase were associated wit esophageal varices ($P < 0.05$). Mean platelet count to portal diameter ratio was $6.64 \pm 0.57$ in patients with esophageal varices and $8.45 \pm 0.79$ in patients without esophageal varices ($P = 0.0001$). Mean platelet to portal vein diameter ratio in patients with grade 1 varices was $5.92 \pm 0.36$ and $6.90 \pm 0.63$ in patients with grade 2 and 3 varices ($P = 0.028$). In logistic regression analysis, Platelet count to portal diameter ratio was independently associated with the presence of esophageal varices ($P < 0.0001$).

**Conclusion:** Platelet count to portal vein diameter ratio can be used as a novel non invasive predictor of esophageal varices in patients with liver cirrhosis. It may also applicable to differentiate grade of esophageal varices in cirrhotic patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0583 RECENT TREND OF VARICEAL BLEEDING IN PATIENTS WITH PORTAL HYPERTENSION AND ITS TREATMENTS

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**Introduction:** Esophageal varices are the most common complication of cirrhosis. Ectopic varices are portosystemic collaterals along the digestive tract outside the gastroesophageal region and are unusual and their frequency has been increasing on a current survey in Japan. In this study, we investigated recent trend of variceal bleeding in patients with portal hypertension and its treatments including ectopic varices.

**Aims & Methods:** One hundred fourteen patients with variceal bleeding and portal hypertension were evaluated retrospectively at Sapporo Kosei Hospital, Japan, from December 2012 to August 2015.

**Results:** Sites of variceal bleeding were as follows; esophageal varices in 56, cardiac varices in 15, fundal varices in 8, and ectopic varices in 35. Ectopic varices were rectal varices in 20, duodenal varices in 4, jejunal varices in 3, gastric body varices in 6 and stomal varices in 2. One hundred thirteen of 114 patients had stigmata of recent bleeding at endoscopy. Patients underwent endoscopic procedures interventional radiology and hemostatic rate was 113 of 114 cases (99.1%). Endoscopic band ligation (EBL) was successfully performed for 49 esophageal varices and endoscopic injection sclerotherapy using 5% ethanolamine oleate (EO) for 5, and EBL plus EIS for 2, respectively. EBL was performed successfully for 6 cardiac varices and EIS using EO for 6, and EBL plus EIS for 3, respectively. EIS using cyanoacrylate was successfully performed for 7 fundal varices and EIS using EO for 1. EIS using EO was performed successfully for 14 rectal varices and EBL for 4, and EBL plus EIS for 2, respectively. EIS using cyanoacrylate was successfully performed for 3 duodenal varices and EIS plus balloon-occluded retrograde transvenous obliteration for 1. EIS using cyanoacrylate was successfully performed for 2 jejunal varices, however, jejunal variceal patient who underwent percutaneous transhepatic obliteration died 2 days after treatment due to poor condition. EBL was successfully performed for 6 gastric body varices. Percutaneous sclerotherapy using EO was successfully performed for 2 stomal varices. No significant complications were observed.
**Conclusion:** Ectopic varices in patients with portal hypertension are considered to be the cause of hemorrhage presenting with gastrointestinal bleeding, and recently, their frequency has been increasing. Endoscopic treatments and interventional radiology have been performed successfully and safety for variceal bleeding including ectopic varices.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0584 REGENERATE: A PHASE 3, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED MULTICENTER STUDY OF OBETICHOLIC ACID THERAPY FOR NONALCOHOLIC STEATOHEPATITIS

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**Introduction:** Nonalcoholic Steatohepatitis (NASH) is a slowly progressive chronic liver disease without approved therapies. Patients with NASH and fibrosis are at high risk of increased mortality. Obeticholic Acid (OCA) is a selective and potent farnesoid X receptor (FXR) agonist, that has been shown to improve liver histology, including NAFLD activity score (NAS) and fibrosis, in a Phase 2 clinical trial (FLINT). Furthermore in FLINT, OCA treated patients had significant improvements in select liver biochemistries, markers of inflammation, and select cardiometabolic parameters.
**Aims & Methods:** The ongoing, randomized, global, Phase 3 study REGENERATE, will further evaluate the effect of OCA on liver histology and clinical outcomes in patients with biopsy-confirmed NASH with stage 2–3 fibrosis. 2065 patients will be randomized 1:1:1 to 10 mg OCA, 25 mg OCA or placebo, each added to standard of care. An interim analysis at 18 months will evaluate the effect of OCA on liver histology. Total study duration is driven by time required to accrue a total of 264 outcome events and is estimated to be ~6 years. Safety assessments will include adverse events (AEs), adjudicated cardiovascular events, and hepatic events as well as laboratory assessments. The effect of OCA on NASH and fibrosis severity will also be assessed by multiple noninvasive methods (FIB-4, APRI, transient elastography, magnetic resonance elastography, etc.).
**Results:** The co-primary liver histology endpoints at 18 months include: (I) improvement in fibrosis by ≥1 stage with no worsening of NASH and (II) resolution of NASH with no worsening in fibrosis stage. Further, confirmation of clinical benefit of OCA will be assessed at the end of the study by comparing the time to first occurrence of any of the following adjudicated events: histological progression to cirrhosis; uncontrolled ascites; hospitalization for: variceal bleed, hepatic encephalopathy or spontaneous bacterial peritonitis; hepatocellular carcinoma; liver transplant or eligibility for liver transplant (defined by model for end stage liver disease (MELD) score ≥15); and death.
**Conclusion:** REGENERATE is the first pivotal study in NASH, designed in conjunction with FDA and meant to support approval of OCA for NASH with fibrosis. This robust Phase 3 study is designed to evaluate the effect of OCA on liver histology and effects on progression to cirrhosis, liver-related clinical outcomes and mortality.
**Disclosure of Interest:** V. Ratziu: Advisory Committees or Review Panels: GalMed, Abbott, Genfit, Enterome, Gilead; Consulting: Tobira, Intercept, Exalenz, Sanofi-Synthelabo, Boehringer-Ingelheim
A.J. Sanyal: Ad Com/Review: BMS,Gilead, Genfit, Abbott, Ikaria, Exhalenz; Consult: Salix, Immuron, Exhalenz, Nim-bus, Genentech, Echosens, Takeda, Merck, Enanta, Zafgen, JD Pharma, Islet Sciences; Research Supp: Salix, Genentech, Intercept, Ikaria, Takeda, GalMed, Novartis, Gilead, Tobira
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## P0585 RISK FACTORS FOR OVERT HEPATIC ENCEPHALOPATHY AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN PATIENTS WITH LIVER CIRRHOSIS

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**Introduction:** Transjugular intrahepatic portosystemic shunt (TIPS) is gradually widely applied in the treatment for variceal bleeding and refractory ascites in patients with liver cirrhosis. Although the patients are carefully selected before the operation, hepatic encephalopathy (HE) is still the main complication of TIPS. However, the risk factors for HE after TIPS procedure were seldom studied.
**Aims & Methods:** This study aims to investigate the risk factors for overt HE within 6 months after undergoing TIPS. The patients with liver cirrhosis who received TIPS in our department during 2014–2015 were screened and reviewed. The occurrence of HE and its first episode time during 6 months after TIPS were recorded. In addition, the age, gender, underlying chronic liver disease, data of the complete blood cell count, liver function test, blood ammonia, renal function test, electrolyte and prothrombin time (PT) before TIPS performance were recorded, and Child-Pugh grade and MELD score were also obtained. Furthermore, Cox proportional hazard regression model was utilized to determine the hazard ratios (HRs) of factors described above for overt HE within 6 months after undergoing TIPS.
**Results:** 102 patients were screened, 28 patients were excluded for incomplete data, and 74 patients (gender: male/female 52/22; age: 53.1 ± 11.6 years; Child-Pugh grade: A/B 34/40; MELD score: 5.87 ± 4.50) were finally included in this study. 60 patients and 14 patients received TIPS for variceal bleeding and refractory ascites, respectively. 26 patients (35.1%) experienced overt HE within 6 months after receiving TIPS, with a median first episode time of 21.5 days. The HRs of factors for overt HE were as below: age 1.100 (95% CI: 1.011–1.198, p = 0.028), gender 0.042 (0.001–1.233, 0.066), underlying liver disease [hepatitis virus B infection 8.500 (0.722–100.127, 0.089), hepatitis C infection 19.576 (0.467–821.219, 0.119), alcohol 0.080 (0.004–1.654, 0.102), primary biliary cholangiolitis 2657.450 (11.316–624053.3, 0.005), others 3.307 (0.035–313.085, 0.606)], erythrocyte 10.885 (0.850–139.392, 0.067), leukocyte 0.890 (0.432–1.834, 0.753), platelet 1.018 (0.985–1.051, 0.295), direct bilirubin 1.746 (1.031–2.959, 0.038), indirect bilirubin 0.912 (0.800–1.040, 0.170), alanine transarninase 1.001 (0.933–1.074, 0.980), aspartate aminotransferase 0.912 (0.826–1.006, 0.066), albumin 1.242 (0.991–1.558, 0.060), alkaline phosphatase 1.044 (1.015–1.073, 0.002), blood ammonia 1.030 (0.989–1.072, 0.160), blood urea nitrogen 0.993 (0.689–1.264, 0.656), creatinine 0.948 (0.896–1.003, 0.064), blood sodium 0.837 (0.609–1.151, 0.273), blood potassium 1.314 (0.076–22.600, 0.851), PT 18.422 (1.664–203.986, 0.018), Child-Pugh grade 1.397 (0.333–5.865, 0.648) and MELD score 4.127 (0.117–145.049, 0.435).
**Conclusion:** Age, primary biliary cholangiolitis, direct bilirubin, alkaline phosphatase and PT are the risk factors for overt HE in a 6-month follow-up after TIPS procedure in patients with liver cirrhosis. However, Child-Pugh grade and MELD score are not the risk factors for overt HE after TIPS performance in well-selected patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0586 ACUTE KIDNEY INJURY IN HOSPITALIZED PATIENTS WITH CIRRHOSIS: ASSOCIATION WITH MORTALITY AT 30 DAYS

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**Introduction:** Acute kidney injury (AKI) occurs in about 20% of hospitalized cirrhotic patients. The Acute Kidney Injury Network (AKIN) defined AKI as a percentage increase in serum creatinine (sCr) of more than or equal to 50% from the stable baseline value in < 3 months or by an absolute increase in sCr of 0.3 mg/dl in < 48 h.
**Aims & Methods:** Retrospective analysis of cirrhotic patients hospitalized in our department during 2 years. Definition of AKI and staging according to AKIN criteria. Classification of etiology of AKI as pre-renal, parenchymal and hepatorenal syndrome. Evaluation of outcome of AKI (regressive, persistent, progressive). Analysis of association between AKI and mortality at 30 days.
**Results:** 95 patients, 85.3% male, mean age 62.4 years. The main etiologies of cirrhosis were: alcoholic in 71.6% and hepatitis C virus in 14.7%. AKI was present in 42.1% of the patients. Regarding staging: 17.9% AKI 1, 14.7% AKI 2 and 9.5% AKI 3. Etiology of AKI: pre-renal in 75%, parenchymal in 12.5% and hepatorenal syndrome in 12.5%. Concerning AKI outcome: regressive in 72.5%, persistent in 12.5% and progressive in 15%. More patients with AKI were admitted in intensive care unit (17.5%) than patients without AKI (1.85%) (p = 0.007). There were no differences in gender, age, etiology of cirrhosis or Child-Pugh score between patients with or without AKI. In univariate analysis, mortality at 30 days was associated with AKI, Child-Pugh C and infection (p < 0.05). Mortality correlated with AKI outcome (Rs = 0.440; p = 0.000). In multivariate analysis, mortality at 30 days was associated with AKI (p = 0.001; OR = 10.38) and Child-Pugh C (p = 0.018; OR = 4.89).
**Conclusion:** In patients with cirrhosis, AKI was associated with 30-day mortality. Progression of AKI was also associated with a worse outcome. It is therefore essential to early identify the development of AKI and start an adequate treatment to improve outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0587 HEPATITIS C VIRUS INFECTION TREATMENT WITH SOFOSBUVIR-LEDIPASVIR: SUSTAINED VIROLOGIC RESPONSE PREDICTING FACTORS

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**Introduction:** Direct-acting antivirals (DAA) have revolutionized the treatment of hepatitis C virus (HCV) infection, with the available clinical trials showing high sustained virologic response (SVR) rates with short treatment regimes, convenient pharmaceutical forms and high tolerability when compared to previous treatment options. However, additional studies are still necessary in order to evaluate the real tolerability of these agents in the daily clinical practice.

**Aims & Methods:** Our objective was to assess the efficacy and safety of Sofosbuvir-Ledipasvir treatment for HCV-infected patients in the daily practice of a tertiary care centre, as well as to identify SVR predicting factors, in order to ascertain if certain subgroups of patients may be in higher risk of HCV relapse. The group of patients with HCV treated with Sofosbuvir-Ledipasvir between February 2015 and January 2016 at our centre was analyzed.

**Results:** Our sample included 172 patients, 113 males (65.7%) and 59 females (34.3%), with a mean age of 55 years (32–84 years). 117 patients (68%) underwent treatment for 12 weeks and the remaining 55 (32%) for 24 weeks, with 16 patients (9.3%) having concomitant administration of Ribavirin. Genotype distribution was the following: genotype 1 – 77.3% (133/172), genotype 3–2.9% (5/172), genotype 4 – 19.2% (33/172), genotype 5–0.6% (1/172). 75 patients (43.6%) were treatment-naïve. Distribution according to fibrosis stages was as follows: F0 0.6% (1/172), F1 15.7% (27/172), F2 32.6% (56/172), F3 24.4% (42/172), F4 26.7% (46/172). Regarding treatment response rates, 86.6% (149/172) of patients had Rapid Virological Response (RVR), with 30 patients having $<15$ IU/mL viral load, and 96.5% (166/172) of patients had End of Treatment Response (ETR). The global SVR rate was 94.2% (162/172), with the following distribution according to genotype and fibrosis stage: genotype 1–96.2% SVR (98% (100/102) for $\leq$F3 patients and 90.3% (28/31) for F4 patients), genotype 3–80% SVR (4/5 F4 patients), genotype 4 – 87.9% SVR (100% (23/23) for $\leq$F3 patients and 60% (6/10) for F4 patients – only one relapse, one stop treatment for adverse event and two dies for no treatment related event) and genotype 5–100% SVR (1/1 $\leq$F3 patient). Patients with genotype 1 or genotype 4 HCV infection were analyzed in order to identify possible SVR predicting factors (genotypes 3 and 5 were not considered for this analysis due to their reduced proportion in our sample). There was a statistically significant association between SVR and fibrosis stage (98.4% SVR in $\leq$F3 patients and SVR 82.9% SVR in F4 patients, $p < 0.001$) and between SVR and ETR ($p < 0.001$). Moreover, there was a statistically significant association between SVR and RVR when $<15$ IU/mL was considered as negative viral load ($p = 0.005$) but not if $<15$ IU/mL was considered as positive viral load ($p = 0.075$). No association was identified, in our sample, between SVR and naïve status or IL28B ($p = 0.993$ and $p = 0.880$, respectively). Mild adverse events were reported by 35 patients (19.7%), with headache being the most common (6.2% of patients). Two adverse events lead to stop treatment at first week treatment (pancreatitis and diarrhea).

**Conclusion:** In our sample of HCV-infected patients, treatment with Sofosbuvir-Ledipasvir was well tolerated and achieved SVR in more than 98% of non-cirrhotic patients. Fibrosis stage $\leq$F3, ETR and RVR (considering $<15$ IU/mL as negative viral load) were associated to SVR.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0588 TOLL-LIKE RECEPTOR 7 AND INTERFERON LAMBDA 1 IN CHRONIC HEPATITIS C: RELATION TO VIRUS REPLICATION AND LIVER INJURY

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**Introduction:** Toll-like receptor 7 (TLR7) can recognize single-stranded RNA viruses like hepatitis C virus (HCV) with subsequent induction of different interferon (IFN) types, including IFN lambdas (IFN-λ), which play an important role in antiviral innate immunity.

**Aims & Methods:** The present work was designed to study the role of TLR7 and IFN-λ1 in chronic hepatitis C (CHC) in relation to virus replication and liver injury. Forty-two treatment-naive patients with CHC and 20 healthy subjects were included in the study. Circulating TLR7-expressing peripheral blood mononuclear cells (PBMC) were identified by color flow cytometry and were expressed as percentages of total lymphocyte count. Quantification of IFN-λ1 levels in serum was performed using enzyme-linked immunosorbant assay. Liver biopsies were examined for assessment of histological activity grade and fibrosis stage according to METAVIR scoring system, and steatosis grade. Immunohistochemical staining was performed using antibodies against TLR7 and IFN-λ1 and was scored semi-quantitatively. The hepatic expression of TLR7 and IFN-λ1 was further classified into: low expression (score 0 or 1) and high expression (score 2 or 3).

**Results:** The percentages of circulating TLR7-expressing PBMC and serum IFN-λ1 levels showed significant increases in patients with CHC compared to healthy subjects ($P = 0.025$ and $P < 0.001$ respectively) and were positively correlated ($P < 0.001$). The hepatic TLR7 and IFN-λ1 expression was low in 35.7% and 23.8% of patients respectively; and was high in 64.3% and 76.2% of patients respectively. The patients with low hepatic TLR7 and IFN-λ1 expression showed significant decreases in the percentages of circulating TLR7-expressing PBMC and serum IFN-λ1 levels; and showed significant increases in serum aminotransferases, viral load and METAVIR histological activity grade and fibrosis stage compared to patients with high hepatic expression ($P < 0.01$). The expressions of TLR7 and IFN-λ1 in the liver were positively correlated in HCV-infected patients ($P < 0.001$).

**Conclusion:** Dysregulation of TLR7/IFN-λ1 signaling pathway seems to play an important role in viral replication and HCV-related liver injury and could be a potential therapeutic target in chronic HCV infection.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0589 SOFOSBUVIR/SIMEPREVIR PLUS A FLAT DOSE OF RIBAVIRIN IS EFFICACY AND SAFETY IN ELDERLY GENOTYPE 1 CIRRHOTIC PATIENTS: A REAL WORLD STUDY

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**Introduction:** The proportion of HCV infected patients over age 65 years in Western countries is increasing. This growth and the advent of new antiviral therapy bring us to consider which is the efficacy and safety in the ''real world'' of a combination of Sofosbuvir and Simeprevir (SOF/SMV) plus a flat dose of ribavirin (RBV) in elderly patients compared to younger patients.

**Aims & Methods:** This study was a multicenter, real-world investigation of once daily treatment with SOF 400 mg+ SMV 150 mg with a flat dose of RBV 800 mg/day for a duration of 12 weeks in treatment naïve or experienced HCV genotype 1-infected patients with compensated cirrhosis. Patients were divided into two groups by age: Group I with less than 65 years of age and Group II aged more than 65 years

**Results:** Of the 262 patients enrolled in the study, 130 (49.6%) were $>65$ years of age (Group II) and 32 $<65$ (Group I). HCV genotype 1a was more frequent in Group I patients compared to Group II (25% vs 5.4% $p < 0.0001$) Sustained virological response at week 4 (SVRw4) and week 12 (SVRw12) was achieved by 94.7% (125/132) of those aged $<65$ years and 97.7% (127/130) of those $>65$. Diabetes was the most common comorbidity in patients $>65$ years compared to younger patients (26.2% vs 12.1% $p < 0.03$) but, this comorbidity did not affect SVR overall. Hepatocellular carcinoma in the Milano criteria was more common in older vs younger patients (16.9% vs 4.5% $p < 0.001$). The most common adverse event (AE) in older patients was a grade 2 anemia (36.2% vs 20.6% $p < 0.01$) but no interruption of antiviral treatment due to anemia was recorded among the older.

**Conclusion:** SOF/SMV plus a daily flat dose of RBV 800 mg for a period of 12 weeks was highly effective and safe in older patients with HCV genotype 1 and cirrhosis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0590 DIRECT OBSERVED THERAPY OF CHRONIC HEPATITIS C WITH INTERFERON-FREE ALL-ORAL REGIMENS AT A LOW-THRESHOLD DRUG TREATMENT FACILITY – A NEW CONCEPT FOR TREATMENT OF PATIENTS WITH BORDERLINE COMPLIANCE RECEIVING OPIOID SUBSTITUTION THERAPY

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**Introduction:** An important subgroup of people who inject drugs (PWID) receives opioid substitution therapy (OST) under direct observation of a physician or nurse at a low-threshold drug treatment facility or pharmacy on a daily basis. Most of these patients suffer from psychiatric comorbidities and are reluctant or unable to go to specialized hepatitis centers. Our hypothesis was that chronic hepatitis C in these difficult-to-treat patients could be optimally managed if modern, interferon-free regimens were applied together with OST under direct observation of a physician or nurse at a low-threshold drug treatment facility.
**Aims & Methods:** Fifty-two PWID with chronic hepatitis C and borderline compliance (male/female: 41/11; mean age: 39.0 ± 9.7 years; genotype (GT) 1/3/4: 41/10/1) started interferon-free treatment of chronic hepatitis C at the "Ambulatorium Suchthilfe Wien" – a low-threshold drug treatment facility in Vienna, Austria. Four patients were coinfected with HIV and 13 had liver cirrhosis. Patients received antiviral treatment together with OST under direct observation of a physician or nurse. For each patient, the individual treatment regimen was selected according to genotype, fibrosis stage, pretreatment, HIV-status and current reimbursement policy of insurances.
**Results:** Following this concept of directly observed therapy, adherence to antiviral therapy was excellent: Only one scheduled date, out of 3.228 dates (0.03%), for ingestion of the antiviral therapy in combination with OST was missed by the 52 patients. Till now, 23 patients (male/female: 20/3; mean age: 39.3 ± 7.0 years; GT1/3/4: 18/4/1; liver cirrhosis present in 7 patients) have completed treatment and a 12-week follow-up period. Virologic healing of hepatitis C infection (sustained virologic response, SVR12) could be confirmed in all 23 patients (SVR12 rate: 100%).
**Conclusion:** Directly observed therapy of chronic hepatitis C with interferon-free all-oral regimens at a low-threshold drug treatment facility represents a promising new concept for treatment of patients with borderline compliance receiving OST. By this concept chronic hepatitis C can be cured in a group of difficult-to-treat patients, who are unable to be treated at hepatologic centers. It should be stressed that successful treatment of these patients is not only beneficial for themselves but also for the general population because further transmission of the virus may be prevented.
**Disclosure of Interest:** M. Gschwantler: Michael Gschwantler participated in advisoy boards and received speaking fees from Abbvie, BMS, Gilead Sciences, MSD and Janssen
All other authors have declared no conflicts of interest.

## P0591 PROMOTION OF INTRA-HOSPITAL REFERRAL OF HEPATITIS B AND C VIRUS CARRIERS TO HEPATOLOGY SPECIALISTS BY ELECTRONIC MEDICAL RECORD-BASED ALERT SYSTEM: A CASE STUDY AT A UNIVERSITY HOSPITAL

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**Introduction:** Due to advances in antiviral therapy, most patients with chronic viral hepatitis have become treatable. However, because most patients do not have subjective symptoms, there are still a number of hepatitis virus carriers who are not aware of their infection. Although testing for the hepatitis B and C virus (HBV or HCV) is performed in daily practice as a preoperative or pretransfusion screening, it remains unclear whether intra-hospital collaboration regarding hepatitis virus carriers identified by the screening testing occurs appropriately in non-hepatology departments even within a large hospital, such as our university hospital.
**Aims & Methods:** Osaka City University Hospital (having 982 beds in 24 wards) developed an alert system in April 2013 to promote referral of hepatitis B surface antigen (HBsAg)-positive or anti-HCV-positive patients to the Department of Hepatology through electronic medical records. Additionally, we changed the preoperative assessment manual of the Department of Anesthesiology to promote the referral of patients who tested positive to the Department of Hepatology. In this study, we investigated the status of hepatitis virus testing in fiscal 2012, the change in the number of referrals related to hepatitis viruses to the Department of Hepatology between the fiscal years 2012 and 2013, the distribution of patients referred in fiscal 2013, and the subsequent clinical courses of the patients following these referrals.
**Results:** In fiscal year 2012, before the introduction of the system, HBsAg screening testing was performed in 13,004 cases, and anti-HCV was performed in 12,374; 450 (3.46%) patients were positive for HBsAg, and 711 (5.75%) were positive for anti-HCV. Positive results in both tests were found most frequently in the Department of Hepatology, followed by surgery-related departments, such as the Department of Orthopedics, Ophthalmology, and Otolaryngology. Since the introduction of the new system, the number of intra-hospital referrals regarding hepatitis virus infections increased from 18.8 ± 5.7 to 29.0 ± 4.5 per month. A steady stream of referrals originated from departments in which there were more patients who tested positive for the hepatitis virus. Some referred patients had progressed to cirrhosis or hepatocellular carcinoma while they were unaware of the infection.
**Conclusion:** This electronic medical record-based alert system is useful for promoting the intra-hospital referral of hepatitis virus carriers who are detected by screening tests to hepatology specialists and is thus considered to be important in the appropriate management of chronic viral hepatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0592 CHANGES IN LIPID PROFILE WITH TREATMENT OF HEPATITIS C WITH DIRECT-ACTING ANTIVIRALS

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**Introduction:** Chronic infection with hepatitis C virus (HCV) is associated with both a disturbed intrahepatic lipid metabolism and an altered pattern of circulating lipoproteins.
**Aims & Methods:** We aimed to evaluate the impact of treatment of hepatitis C with direct-acting antivirals without interferon (DAA) on serum lipid profile. Analysis of all patients with chronic hepatitis C treated with DAA in one center, from whom measurements of total cholesterol (TChol), low-density lipoproteins (LDL), high-density lipoproteins (HDL) and/or triglycerides (TG) were performed at first day of therapy (baseline), end-of-treatment (EOT) and/or 12 weeks after EOT (PT12). Patients on lipid lowering drugs or with detectable HCV viral load on PT12 were excluded. Hepatitis C treatment regimens were selected according to national and/or EASL recommendations. Statistical analysis performed with STATA® v12.1 and Excel® 2010.
**Results:** Forty-two patients were analysed, 73.8% (31/42) male, median age 55 years (41;72), 14.3% (6/42) of them obese (IMC > 30 kg/m$^2$). Twenty-five (59.5%) patients had HCV genotype 1, 14 patients had HCV genotype 3, and 3 patients had HCV genotype 4. Twenty-nine patients had cirrhosis. All patients were treated with sofosbuvir/ledipasvir, with or without ribavirin, during 12 or 24 weeks, and had HCV viral load < 15UI/mL on EOT. During treatment with DAA (from baseline to EOT), there was a significant rise in mean TChol (from 159.4 mg/dL to 182.5 mg/dL; n = 41; $p < 0.001$) and LDL (from 90.3 mg/dL to 116.4 mg/dL; n = 40; $p < 0.001$), whereas TG decreased significantly (from 100.7 mg/dL to 83.5 mg/dL; n = 41; $p < 0.001$) and HDL levels remained stable (from 45.2mg/dL to 46.1 mg/dL; n = 40; p = 0.63). On PT12, mean TChol levels (171.2 mg/dL vs 151.1 mg/dL; n = 20; $p < 0.01$) and mean LDL levels (105.8 mg/dL vs 79 mg/dL; n = 19; $p < 0.01$) remained significant higher than on baseline; while HDL levels (46.8 mg/dL vs 48.7 mg/dL; n = 19; p = 0.60) and TG levels (94.8 mg/dL vs 91.6 mg/dL; n = 18; p = 0.77) were similar to those on baseline. Similar trends were observed on sub-analyses for HCV genotype and disease stage.
**Conclusion:** We observed significant changes in lipid profile with treatment of hepatitis C with direct-acting antivirals. Further studies are needed, investigating possible influence of treatment regimen and if the observed changes in lipid profile persist in the long-term.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0593 EMERGENCE OF MULTIDRUG-RESISTANT HEPATITIS C VIRUS DURING INTERFERON-FREE THERAPY WITH ASUNAPREVIR AND DACLATASVIR AFTER SIMEPREVIR-BASED TRIPLE THERAPY FOR RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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**Introduction:** The treatment for hepatitis C virus (HCV) has dramatically changed with the introduction of direct-acting antivirals (DAAs). The efficacy and safety of interferon-free therapy after liver transplantation have been recently confirmed[1)]. However, the emergence of HCV resistance to DAAs is a major obstacle of interferon-free therapy, especially in patients who had prior DAA-containing therapy.
**Aims & Methods:** This study aimed to clarify the dynamic changes of resistance-associated variants during interferon-free therapy with asunaprevir and daclatasvir after simeprevir-based triple therapy for recurrent hepatitis C after liver transplantation. Daclatasvir (60 mg/day) and asunaprevir (200 mg/day) were administered to 15 patients with recurrent hepatitis C genotype 1 b after liver transplantation. Efficacy and safety of this therapy were clarified. Resistance-associated substitutions in NS3 and NS5A region of HCV genome were analyzed before and after the therapy in patients who did not achieve sustained virological response (SVR) by using the ultra-deep sequencing analysis.
**Results:** Eight patients were treatment-naive, and 7 patients were treatment-experienced with peginterferon and ribavirin in 3 patients, and with simeprevir, peginterferon, and ribavirin in 4 patients. SVR was achieved in 9 of the 15 patients, resulting in the 60% SVR rate. In the 6 non-SVR patients, 4 had simeprevir-based triple therapy before this interferon-free therapy. Although none of the 4 patients had resistance-associated substitutions at D168 of NS3 region before simeprevir-based triple therapy, the D168-resistant associated variants became dominant HCV clones at the viral breakthrough or relapse in the simeprevir-based therapy. At 4 to 9 months after the termination of simeprevir administration, interferon-free therapy with asunaprevir and daclatasvir was

initiated. Emergence of multidrug-resistant HCV with resistance-associated substitutions at D168 of NS3 region and at L31, L32, and/or Y93 of NS5A region was observed in the 4 patients during asunaprevir and daclatasvir administration. Sofosbuvir and ledipasvir for 12 weeks successfully eradicated the multidrug-resistant HCV in a case.
**Conclusion:** Interferon-free therapy with asunaprevir and daclatasvir for 24 weeks was well tolerated and resulted in 60% of SVR in liver transplant recipients with HCV genotype 1 b infection. Resistance-associated variants induced by the prior simeprevir administration resulted in the emergence of multidrug resistant HCV and the treatment failure of this interferon-free therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0594 NON-INVASIVE HEPATIC FIBROSIS EVALUATION ON HEPATITIS C – THE IMPACT OF NEW TREATMENTS

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**Introduction:** Hepatic fibrosis occurs in response to sustained hepatic injury. Withdrawal of the aggressive agent may allow regression of the fibrotic process.
**Aims & Methods:** Aims: Assess the impact of new Hepatitis C treatments in hepatic fibrosis determined by non-invasive biologic scores. Methods: Included patients that systematically concluded treatment with sofosbuvir/sofosbuvir + ledipasvir. Four non-invasive biologic scores (Forns Index, APRI, GUCI e FIB-4) were calculated before the treatment (T0), at the fourth week of treatment (T4) and at the end of treatment (Tfinal). Statistical analysis was preformed with SPSS v21.0, and a value of $p < 0.05$ was considered statistically significant.
**Results:** Twenty eight patients included. Genotype 1 was the most frequent in 64.3%. Previous treatment was performed in 57.1% of patients. At the beginning of treatment, 32.1% of patients were classified as fibrosis stage F4. We found statistically significant differences between score values at T0 and T4 as well as between T0 and Tfinal, as accessed by Forns Index (6.85 vs 6.09, $p < 0.01$ and 6.85 vs 5.92, $p < 0.01$), APRI (1.83 vs 0.48, $p < 0.01$ and 1.83 vs 0.51, $p < 0.01$), GUCI (2.03 vs 0.55, $p < 0.01$ and 2.03 vs 0.57, $p < 0.01$) and FIB-4 (2.71 vs 1.53, $p < 0.01$ and 2.71 vs 1.56, $p < 0.01$). No differences were found between the values of fibrosis at T4 and Tfinal for any score. Only for FIB-4 score did we found significant differences in the variation of score between patients with initial fibrosis F1–3 vs F4 (0.71 vs 2.1, $p = 0.03$).
**Conclusion:** New treatments associate with significant and precocious variation in non-invasive biologic scores for hepatic fibrosis. It becomes relevant to compare these findings with non-invasive physical scores and, eventually, with histology, to assess if analytic improvement translates, in equal proportion, in parenchymal/histologic improvement.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0595 RISK FACTORS FOR PRIMARY SCLEROSING CHOLANGITIS RECURRENCE AFTER LIVER TRANSPLANTATION

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**Introduction:** Primary sclerosing cholangitis (PSC) is a chronic liver disorder of unknown etiology, characterized by inflammation, fibrosis and stenoses. The disease may progress to cirrhosis and eventually to liver failure and death. For those who develop end – stage liver disease, orthotopic liver transplantation (OLT) remains the only effective treatment currently available. However, recurrent form of PSC (rPSC) often appears in patients after OLT and may eventually lead to graft loss and liver re – transplantation (re – OLT). The aim of our retrospective study was to identify risk factors for rPSC.
**Aims & Methods:** A total number of 115 orthotopic liver transplantations for PSC were performed at Institute for Clinical and Experimental Medicine, Prague, Czech Republic between July 1994 and May 2015. The diagnosis of rPSC was based on histology and cholangiographic findings. We retrospectively analyzed medical records of all PSC patients from our computed database. Only patients with a proper record of pre – OLT ($\leq$12 months) colonoscopy and those monitored for a time period of $\geq$ 60 months post – OLT were included. Input data were analyzed using JMP statistical software. Student's t-test, Fisher's exact test and nominal logistic regression were used to assess the data. A p – value $< 0.05$ was considered as statistically significant.
**Results:** After applying inclusion/exclusion criteria, we analyzed a cohort of 47 patients. 31 were male, 16 female, with median age of 36 (range 15–68) and median follow – up 122 months (range 60–249) after OLT. In 21/47 (44.7%) patients, rPSC was diagnosed during the follow – up. Two patients underwent re – OLT (after 103 and 116 months respectively, both for rPSC). According to performed univariate analysis, presence of de – novo colitis ($p = 0.0002$; OR 27.50, 95% CI 3.13 – 241.94) and OLT for overlap with autoimmune hepatitis (PSC/AIH) ($p = 0.0133$) were significantly associated with rPSC. Presence of HLA-DRB1*04 in the recipient was identified as protective factor for rPSC ($p = 0.0287$). In case of de – novo colitis, statistical significance was further confirmed by nominal logistic regression analysis ($p = 0.0094$; OR 22.00, 95% CI 2.04 – 591.60). Neither gender, nor age, CMV infection, acute cellular rejection (ACR), corticoresistant ACR, use of OKT3, presence of HLA-DRB1*08, history of cholangiocarcinoma, cold ischemia time and length of corticosteroids use were significantly associated with rPSC.
**Conclusion:** Recurrent PSC is an important clinical entity with high prevalence in patients after OLT. De – novo colitis is a significant risk factor associated with rPSC, along with PSC/AIH overlap, while presence of HLA-DRB1*04 in the recipient appeared to have a protective effect on rPSC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0596 HEPATIC COMPUTED TOMOGRAPHY VOLUMETRY FOR NON INVASIVE PREDICTION OF HEPATIC STEATOSIS AND STEATOHEPATITIS IN LIVING RELATED LIVER TRANSPLANTATION

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**Introduction:** Macrovesicular hepatic steatosis is associated with complications after living related liver transplantation. Therefore, detection of hepatic steatosis in potential organ donors by liver biopsy has an important role to prevent future adverse outcomes. Since liver biopsy is an invasive procedure, several attempts have been made to find a non invasive method for precise estimation of hepatic steatosis.
**Aims & Methods:** This study aimed to investigate the role of hepatic computed tomography (CT) volumetry in detection of hepatic steatosis in living liver donors. A cross sectional study was conducted between August 2012 and August 2015 at Namazi hospital, Shiraz, Iran. Study subjects were healthy individuals who had undergone liver biopsy for evaluation of liver histology as a routine pre-transplant check up before living related liver transplantation. Liver function tests, age, gender, weight, height, fasting plasma glucose, and lipid profile were recorded. Liver biopsy specimens were reviewed by an expert pathologist for hepatic steatosis and steatohepatitis. Spiral abdominal CT scan with intravenous contrast enhancement was performed for all patients. The total volume of liver, volume of left lobe and left lateral segment were recorded. These measures were compared in those with and without hepatic steatosis/steatohepatitis.
**Results:** Totally 177 individuals were included. Sixty four individuals had biopsy proven macrovesicular steatosis. Mean age of individuals with and without hepatic steatosis in liver biopsy were $32.39 \pm 6.53$ years and $31.82 \pm 6.88$ years respectively ($P = 0.6$). In univariate analysis, weight, serum triglyceride, cholesterol, alanine aminotransferase, alkaline phosphatase and fasting plasma glucose were associated with hepatic steatosis ($P < 0.05$). Mean total volume of the liver was $1530.1 \pm 273.3$ $cm^3$ in those with hepatic steatosis and $1395.4 \pm 231.4$ $cm^3$ in those without hepatic steatosis ($P = 0.003$). Mean volume of left lateral segment of the liver was $221.9 \pm 69.9$ $cm^3$ in individuals with hepatic steatosis and $196.3 \pm 64.7$ $cm^3$ in individuals without hepatic steatosis ($P = 0.039$). In logistic regression analysis, neither total liver volume nor volume of left lateral segment of the liver were predictor of hepatic steatosis ($p > 0.05$). Sixteen individuals had steatohepatitis in their liver biopsy. In univariate analysis, higher weight, serum triglyceride, and alanine aminotransferase were associated with hepatic steatohepatitis ($P < 0.05$). Mean total volume of the liver was $1705.2 \pm 256.5$ $cm^3$ in those with hepatic steatohepatitis and $1419.4 \pm 241.2$ $cm^3$ in those without hepatic steatohepatitis ($P = 0.0001$). In logistic regression analysis, higher total volume of the liver was an independent predictor of hepatic steatohepatitis (OR: 1.005; 95% CI: 1.001–1.010, $P = 0.012$). A cut off value of 1531 $cm^3$ for total volume of the liver was predictor of presence of steatohepatitis in liver biopsy of donors (sensitivity = 83%; specificity = 71%; area under curve = 0.809; P-value = 0.0001).
**Conclusion:** CT volumetry can be considered as a non invasive method for prediction of hepatic steatosis of donors in living related liver transplantation. Higher total volume of the liver is an independent factor that predicts hepatic steatohepatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0597 PARACETAMOL-INDUCED ACUTE LIVER FAILURE IN A PORCINE MODEL IS ASSOCIATED WITH SIGNIFICANT GUT DYSBIOSIS

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**Introduction:** Gut dysbiosis is implicated in chronic liver disease, however little is known in the context of acute liver failure.

**Aims & Methods:** In this study, we investigated the changes in the gut microbiome in a porcine model of paracetamol-induced acute liver failure. We induced acute liver failure in seven weight-matched female pigs (*Sus scrofa domesticus*) with a toxic dose[1] of paracetamol 1 gm/kg intravenously. Signs of acute liver failure were evident at 24hours. Animals were monitored and managed for a total study duration of 48 hours following best practice. Stool specimen was collected upon initiation of paracetamol (T = 0) and after 48 hours (T = 48). Microbiome analysis was accomplished using the method described by Wu et. al[2]. DNA was extracted[3]using a QIAamp DNA stool mini-kit (QIAGEN). Pyrosequencing reads were uploaded onto QIIME software (http://qiime.org/), classified, aligned and processed into phylogenetic trees as described previously[3]. Statistical analysis was performed using UniFrac software (http://bmf.colorado.edu/unifrac); by comparing distances within groups to distances between groups[4]. Comparisons was summarised using the t-statistics and significance assessed using 10000 permutations[3]. Sequencing 16 S rRNA gene pool from specimens was used to identify the microbial landscape in the gut and perform grouping by shared sequence characteristics (taxonomical assignment).

**Results:** In established acute liver failure at 48hrs, OTU (Operational Taxonomic Units) observed at the level of family changes in statistically significant abundance were Ruminococceae and Spirochaetaceae. There was a relative increase in the abundance of Fibrobacter intestinalis, and Ruminococus gnavus at the expense of Lactobacillus genus belonging to Firmicutes phylum. Dysbiosis ratio[5] changed significantly ($p = 0.042$) in paracetamol-induced acute liver failure reflecting a rapid shift in gut microbiome. Between the groups (0 h and 48 h), significant OTU difference at the family level [Analysis of similarities (ANOSIM R): 0.242, p-value: 0.0075; Bray-Curtis metrics], with only marginal differences (chi squared metrics) at genus level but no difference at species levels was observed. Wilcoxon test did not reveal any statistical significant trend (increasing or decreasing) in the gut microbiome biodiversity between groups.

**Conclusion:** In paracetamol-induced acute liver failure in pigs we observe an acute onset significant relative change in the autochthonous taxa without alteration to gut microbiome biodiversity. Dysbiosis ratio changed significantly and rapidly in acute liver failure reflecting imbalance of ''good'' vs ''bad'' bacteria.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0598 THE ROLE OF TIPS IN THE MANAGEMENT OF LIVER TRANSPLANT CANDIDATES

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**Introduction:** Transjugular portosystemic shunt (TIPS) implantation was shown to be effective in controlling variceal re-bleeding and refractory ascites in patients with liver cirrhosis[1,2,3]. However, its impact on the outcome of patients on the liver transplant waiting list is less clear. A recent UNOS database analysis has demonstrated a decreased risk of death in patients with TIPS at listing[4], but the optimal time point for TIPS implantation has not been established.

**Aims & Methods:** Here we aimed to retrospectively assess the outcome of patients undergoing TIPS implantation before (pre-listing) or after (post-listing) listing for orthotopic liver transplantation (OLT) at a tertiary care hospital. We retrospectively identified n = 98 patients with TIPS who were on the OLT waiting list between 01/1993–12/2013. 73 patients (74.5%) received a pre-listing TIPS and 25 patients (25.5%) a post-listing TIPS. A control group (n = 60) was matched to assess the differences in post-transplantation outcome according to underlying disease, sex, BMI and age at listing.

**Results:** More patients with post-listing TIPS (28.0%, 7/25) showed clinical improvement and went off-list than patients with pre-list TIPS (8.2%, 6/73, $p = 0.0119$). A similar proportion of patients with pre-list TIPS (19.2%, 14/73) and post-list TIPS (20.0%, 5/25) died on the OLT waiting list. More pre-list TIPS patients (72.6%, 53/73) than post-list TIPS patients (52.0%, 13/25) finally underwent OLT ($p = 0.0580$). MELD score evolution on the OLT list was similar for patients with pre-list and post-list TIPS (Listing-MELD: $15.7 \pm 0.5$ vs. $14.4 \pm 0.9$, p = n.s.; OLT-MELD: $17.5 \pm 0.8$ vs. $19.5 \pm 1.6$; p = n.s,). Mean OP-time was 348.0 (±12.5) minutes and a median of 3 (IQR 0–7) RBCs transfusions were required during OLT for patients with TIPS vs 337.4 (±9.8) minutes and a median of 5 (1.75–8) for patients without a TIPS. Estimated 1-year post-transplant survival was 86.0% in the pre-list TIPS group, 76.2% in the post-list TIPS group and 91.2% in the control group (log-rank $p = 0.1506$).

**Conclusion:** TIPS implantation represents an important tool for the management of portal hypertension with a favorable one-year post-OLT-survival. TIPS should be placed prior to listing to assess the actual need for listing (less delisting with pre-list TIPS) and to optimize the bridging to OLT (higher OLT-rate with pre-list TIPS).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0599 POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER AFTER LIVER TRANSPLANTATION: LONG TERM SURVIVAL AND THE IMPACT OF SERUM TACROLIMUS LEVEL

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**Introduction:** Post transplant lymphoproliferative disorder (PTLD) is one of the complications that may occur after liver transplantation and threaten both graft and patient survival.

**Aims & Methods:** This study aimed to investigate incidence and survival of PTLD patients after liver transplantation. Shiraz Organ Transplant center is a leading transplant center not only in Iran but also in Middle East and Asia with considerable annual cases of liver transplantation for both adult and pediatric patients. A cross-sectional survey was conducted among adult and pediatric patients (< 18 years) who underwent liver transplantation at Shiraz transplant center, Shiraz, Iran between August 2004 and August 2014. Clinical and laboratory data of patients were collected using a data gathering form containing information regarding age, sex, underlying liver disease, type of allograft (deceased donor, living related donor, split liver transplantation), time of liver transplantation and time of PTLD development, survival of patients from date of liver transplantation, survival after PTLD diagnosis, immunosuppressive regimen and dosage, rejection episodes, EBV status before and after transplantation, presenting sign and symptoms, PTLD histology, multi-organ involvement, modality of treatment, response to therapy, serum level of calcineurin inhibitors including tacrolimus and cyclosporine. Patients received tacrolimus, cyclosporine, mycophenolate mofetile and prednisolone as immunosuppressive therapy during their follow up.

**Results:** There were 40 cases of PTLD in pediatric age group and 13 cases in adult patients. The incidence of PTLD was 6.25% in pediatric patients and 1.18% in adult liver transplant recipients. The post-PTLD survival of patients at 6 months was 75.1% (±SE 6%), at 1 year was 68.9% (±SE 6.5%) and at 5 years was 39.2% (±SE 14.2%). The mean post-PTLD survival in adult patients was $82.94 \pm 18.58$ months. The post-PTLD survival of adult patients at 6 months was 83.9% (±SE 10.4%), at 1 year was 74.6% (±SE 12.8%) and at 5 years was 59.7% (±SE 16.8%). The mean post-PTLD survival in pediatric patients was $42.61 \pm 6.1$ months. The post-PTLD survival of pediatric patients at 6 months was 72.4% (±SE 7.1%), at 1 year was 67.1% (±SE 7.5%) and at 5 years was 24.1% (±SE 18.6%). Multi-organ involvement was significantly associated with lower post-PTLD survival ($104.25 \pm 9.08$ months vs. $27.13 \pm 6.30$ months, $P = 0.002$). EBV-positive patients with PTLD had significantly higher mean survival compared to EBV-negative PTLD patients ($60.58 \pm 7.62$ months vs. $16.72 \pm 5.66$ months, $P = 0.018$). Higher serum tacrolimus level was associated with lower post-PTLD survival in pediatric patients (OR: 1.07; 95% CI: 1.006–1.15; P-value = 0.032) (Table). A serum tacrolimus of 11.1 ng/ml was predictor of post PTLD survival (sensitivity = 90%; specificity = 52%; area under curve = 0.738; P-value = 0.035).

**Conclusion:** Our study is one of the largest series of patients with PTLD after liver transplantation. This study showed that the incidence of PTLD following pediatric liver transplantation was much higher than adult liver transplantation Incidence of PTLD in our liver transplant patients is comparable to other

centers. Transplant physicians may consider adjustment of tacrolimus dose to maintain its' serum level around this cut of point.

**Table:** Cox-regression analysis of association of multiple risk factors and post-PTLD survival of pediatric patients

| | Mean | OR | 95% CI | P-Value |
|---|---|---|---|---|
| Age (years) | 5.05 | 0.94 | 0.82–1.08 | 0.434 |
| Time to PTLD (Months) | 15.63 | 0.96 | 0.91–1.02 | 0.242 |
| Tacrolimus Level | 14.99 | 1.07 | 1.006–1.15 | 0.032 |
| Tacrolimus Dose | 3.81 | 1.06 | 0.67–1.66 | 0.797 |
| Prednisolon Dose | 10.12 | 0.99 | 0.86–1.13 | 0.897 |

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0600 OBLITERATION OF PORTOSYSTEMIC SHUNTS IMPROVES HEPATIC FUNCTIONAL RESERVE

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**Introduction:** Balloon-occluded retrograde transvenous obliteration (B-RTO) has been widely adopted for the management of gastric fundal varices (GV). B-RTO can be a suitable treatment option for refractory hepatic encephalopathy (HE) with large portosystemic shunts (PSS). Percutaneous transhepatic obliteration (PTO) is a useful antegrade obliteration method for PSS that is hard to access by B-RTO. There are many reports that obliteration of PSS leads it to the improvement of the liver function in the short term, however the long-term effects are not well known.

**Aims & Methods:** We retrospectively review the long-term effect on liver functional improvement and the prognosis of the patients who had the obliteration of PSS. We performed PSS obliteration using B-RTO and/or PTO in 63 patients with GV (n = 41) and/or HE (n = 24) between 2005 and 2015 at a single institute. We examined the parameters of hepatic functional reserve such as encephalopathy, ascites, total bilirubin, albumin, prothrombin time, Child-Pugh score, and liver volume in the follow-up period 3, 6, 12, 24, and 36 months after PSS obliteration. We analyzed the survival curve using Kaplan-Meier method, and investigated the preoperative factor which affected a prognosis independently with multivariable analyses.

**Results:** GVs were well-embolized in 40 patients (97.6%), and GV disapeared in all patients successfully treated by B-RTO. PSS in HE patients were well embolized in 20 patients (83.3%). The plasma ammonia level significantly decreased, and HE was improved after PSS obliteration. The serum albumin level was significantly elevated in the long-term follow-up. The median survival was of all cases was 1871 days. Multivariable analyses revealed that cases with cancer and preoperative Child-Pugh B-C grade were predictors of poor prognosis.

**Conclusion:** Significant improvement of the hepatic residual function after PSS obliteration is present in the short term, however, it does not have the permanent effect in all cases. When the PSS obliteration is necessary is the optimal time, however, what we perform it in the time preserved the liver residual function without the cancer is desirable from the viewpoint of long-term survival.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0601 CONTRAST ENHANCED ULTRASOUND AS A FIRST LINE IMAGING METHOD IN THE EVALUATION OF FLL IN DAILY PRACTICE. A LARGE MONOCENTRIC EXPERIENCE

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**Introduction:** Contrast enhanced ultrasound (CEUS) has become the first line imaging method in our center, used for the characterization of focal liver lesions (FLL), after it proved to be a cost-efficient method (1). We present you a monocentric experience in the evaluation of focal liver lesions by CEUS in daily practice routine in our center.

**Aims & Methods:** The retrospective study performed between September 2009-December 2015, included 2037 patients, in whom CEUS was performed. We evaluated **2427** FLL "de novo. The evaluation by CEUS was considered conclusive if the FLL had a typical enhancement pattern following contrast bolus as described in the European Guidelines for the use of CEUS, issued by the European Federation of Societies of Ultrasound in Medicine and Biology (EFSUMB) (2).

**Results:** From the 2427 FLL examined by CEUS, a positive diagnosis of malignant vs. benign could be established by CEUS in **2138/2427, (88.1%)**: 49.9%(1068) benign and 50.1%(1070) malignant, the latter with typical washout pattern in the late phase. In 289/2427 (11.9%) cases, CEUS was inconclusive, other methods being required (CT, MRI or biopsy) for the final diagnosis. From the total of 2427 lesions evaluated by CEUS, we were able to provide the correct classification in 1931 **(79.6%)** of cases. From all the FLLs evaluated by CEUS, 442 (22.9%) were hepatocellular carcinomas; 490 (25.4%) were liver metastases; 373 (19.2%) hemangiomas; 257 (13.4%) focal fatty liver alterations; 75 (3.9%) focal nodular hyperplasia (FNH); 1.2% (22) Adenomas, 82 (4.2%) hepatic cyst; 48 (2.5%) liver abscesses; 80 (4.1%) regenerative nodules; 0.5% (10) Cholangiocarcinoma; 0.1% (2) other malignant lesions; 2.5% (48) other benign lesions.

**Conclusion:** CEUS demonstrated its efficiency as a good first-line imaging method for the characterization of focal liver lesions detected by ultrasound, with a positive diagnosis in 79.6% cases and differentiation between malignant and benign lesions in **88.1%** % cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0602 EVALUATION OF LIVER FIBROSIS USING TRANSIENT ELASTOGRAPHY IN NONALCOHOLIC STEATOHEPATITIS (NASH) PATIENTS

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**Introduction:** The incidence of nonalcoholic steatohepatitis (NASH) has significantly increased in the last years, mainly due to modern lifestyle changes. Liver stiffness measurements by means of Transient Elastography (TE) has been widely accepted as a tool for fibrosis assessment not only in chronic viral liver diseases but also in patients with nonalcoholic steatohepatitis.

**Aims & Methods:** The **aim** of the present study was to assess the severity and the dynamics of liver fibrosis in NASH patients.

**Material and methods**: A retrospective study of 890 patients with nonalcoholic steatohepatitis was conducted. The diagnosis of NASH was established based on: ultrasound examination (moderate or severe liver steatosis- "bright liver" with posterior attenuation); biological tests (increased aminotransferases level); no history of alcohol abuse; negative viral hepatitis B or C markers. In each patient ten LS measurements were performed by means of TE, either with the M (3.5 MHz) probe or with XL (2.5 MHz). In patients in which reliable measurements could not be obtained by M probe, XL measurements were performed in the same session. Reliable measurements were defined as: median value of 10 LS measurements with a success rate (SR) $\geq$60% and an interquartile range (IQR) $<$30%. Using the proposed cut-offs by Wong 2010 [1], NASH patients were divided into 3 categories $<$7.9 kPa (absence of severe fibrosis); values ranging between 7.9 kPa and 9.6 kPa ("gray zone" in which biopsy is recommended); and $>$9.6 kPa (severe fibrosis).

**Results:** Out of 890 patients, reliable measurements by either probe were obtained in 76.5%. Older age, female gender and higher BMI were associated with unreliable TE measurements. The analysis of liver fibrosis distribution was performed in 681 NASH patients with reliable LSM. Using the proposed cut-offs, 69.5% of the patients did not have severe fibrosis, 11.5% had F$\geq$2 fibrosis being in the "gray zone" and 19% had severe fibrosis. In 49 patients the dynamics of fibrosis was evaluated. Over a period of at least 2 years, fibrosis progression was observed in 12.2%, 75.6% had stable fibrosis, and 12.2% had an improvement in fibrosis stage.

**Conclusion:** Approximately 20% of NASH patients had LSM compatible with severe fibrosis, therefore LS assessment should be performed systematically in NASH patients.

**Disclosure of Interest:** I. Sporea: Ioan Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric.
A. Popescu: Alina Popescu received speaker fees from Philips.
R.L.D. Sirli: Roxana Şirli received speaker fees from Philips
All other authors have declared no conflicts of interest.

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## P0603 LIVER AND SPLEEN STIFFNESS ASSESSED BY TRANSIENT ELASTOGRAPHY AND REAL-TIME 2D SHEAR WAVE ELASTOGRAPHY AND ELF™ TEST HAVE VERY GOOD PERFORMANCE FOR NON-INVASIVE DETECTION AND ESTIMATING SEVERITY OF PORTAL HYPERTENSION

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**Introduction:** The aim of this study was to test performance of quantitative elastographic methods and Enhanced Liver Fibrosis (ELF™) test as potential non-invasive tools for assessment of portal hypertension (PH).

**Aims & Methods:** Patients suspected as having compensated advanced chronic liver disease (cACLD) of different aetiologies based on previous clinical diagnostic work-up were considered candidates for invasive approach in order to confirm the aetiology and stage of liver disease as well as to confirm presence and severity of PH. Hepatic venous pressure gradient (HVPG) served as a reference method for assessment of PH and was measured in each patient by standardized transjugular approach (Fig. 1). All patients had been scanned by transabdominal ultrasound prior to HVPG measurement including elastographic assessment of liver and spleen stiffness (LS and SS) by 2 different methods (Transient elastography (TE; Fibroscan®, Echosense) and Real-time 2-dimensional shear wave elastography (RT-2D-SWE; Aixplorer® US system, Supersonic imagine). ELF™ as a representative of serological tests was performed from single blood specimen taken from each study subject and performed according to manufacturer instructions.

**Results:** Twenty (20) patients (14 male; median age 62 (34–74) years; 8 Non Alcoholic Fatty Liver Disease, 6 Alcoholic Liver Disease, 6 other aetiologies; median fibrosis stage 6 (0–6), mean $4.75 \pm 1.7$ according to Ishak) consecutively underwent HVPG measurement (median value 10.25 mmHg (1.5–22.4)). No major adverse event occurred in relation to HVPG procedure. Liver cirrhosis was histologically confirmed in 14/20 (70%) patients, and clinically significant portal hypertension (CSPH$\geq$10 mmHg) in 11/20 (55%). TE used M probe in 55% and XL probe in 45% of patients. LS correlated significantly to HVPG (Spearmann $\rho = 0.863$ $p < 0.0001$ for RT-2D-SWE and $\rho = 0.77$, $p = 0.0001$ for TE). SS showed significant correlation with HVPG as well (Spearmann $\rho = 0.78$; $p = 0.0002$ for RT-2D-SWE and $\rho = 0.69$, $p = 0.0042$ for TE). Correlation between HVPG and ELF test was also significant ($\rho = 0.62$; $p = 0.0046$). Assessment of LS by RT-2D-SWE and TE had excellent performance for differentiation between patients with or without CSPH (LS cut-off 12.6 kPa; Se 90.9%, Sp 87.5%, PPV 90.9%, NPV 87.5%, AUC 0.94 and 10.4 kPa, Se 90%, Sp 88.9%, PPV 90%, NPV 88.9% AUC 0.89 respectively). The same was observed for SS (cut-off 30.2 kPa; Se 60%, Sp 100%, PPV 100%, NPV 63.6%, AUC 0.81 and 41.8 kPa, Se 66.7%, Sp 100%, PPV 100%, NPV 66.7% AUC 0.85 respectively). At cut-off 9.88 ELF test was able to differentiate between patients with or without CSPH (Se 81.2%, Sp 87.5%, PPV 90%, NPV 77.8%, AUC 0.818).

**Conclusion:** Both elastographic and serological tests demonstrated very strong correlation to portal hypertension as assessed by HVPG measurement. Both group of tests, and both LS and SS showed very good performance for non-invasive diagnosis of CSPH, with lower cut-off values than previously published.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0604 OUTCOMES OF RADIOFREQUENCY ABLATION AND MICROWAVE ABLATION IN LIVER METASTASES: A SINGLE CENTER EXPERIENCE

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**Introduction:** Microwave ablation (MWA) and radiofrequency ablation (RFA) have both emerged as promising treatment modalities for liver metastases, but the technical and oncologic differences between these modalities are not fully investigated.

**Aims & Methods:** To evaluate technical success, effectiveness and safety of MWA and RFA in patients with unresectable liver metastases. A retrospective analysis of 42 patients who underwent percutaneous MWA or RFA of liver metastases from 20011 to 2016 at our institution was performed. Peri-interventional and long-term data were reviewed to determine outcomes and patterns of recurrence.

**Results:** A total of 59 tumors were treated, ranging 0.5–4.5 cm in range. Technical success was obtained in all cases. 13 tumors (22%) were treated with MWA and 46 (78%) were treated with RFA. 29 (69%) patients had colorectal metastases, 6 (14.28%) patients had metastatic breast cancer and 7 (16.66%) patients had other types of hepatic metastases. The median follow-up was 300 days. Overall hepatic recurrence rate was 33.2%. Median time to first recurrence was 356 days. There were no complication after MWA while 5 (15.62%) patients in the RFA group had major complication (2 cases of hepatic abscess; 2 cases of arterio-portal fistula and one hematoma). Hepatic recurrence rate was significantly higher in tumors treated with RFA compared to MWA (39.13% versus 7.69%, P: 0.032). However the median follow-up was significantly shorter in the MWA versus RFA treated patients (180 versus 330 days, P: 0.025).

**Conclusion:** Although this was not a matched cohort analysis, overall hepatic recurrences were lower in patients treated with MWA compared to RFA. Longer follow-up time in the MWA may increase the recurrence rate. Moreover MWA seems to be safer than RFA in the long term management of hepatic metastases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0605 VALIDITY OF ALBI-T SCORING MODEL AS A PROGNOSTIC INDICATOR IN EGYPTIAN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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**Introduction:** The Child-Pugh (CTP) score for evaluation of liver function status has limitations as it relies on individual subjective variables as ascites and encephalopathy that are scored based on arbitrarily defined points. The albumin-bilirubin (ALBI) [1] score eliminates the need for the subjective variables required in the CTP grade and offers more precise selection of patients with HCC for treatment allocation and it is now considered a core for other scores as ALBI-T[2] score after incorporating other factor as TNM stage to reflect the extent of the tumor in ALBI-T score.

**Aims & Methods:** This study was conducted on 415 patients with HCC in a tertiary referral center in Egypt. Baseline characteristics including CTP, BCLC, ALBI[1] & ALBI-T[2] scores were determined. Patients were followed up from the time of diagnosis to the date of death or date of data collection if they remained alive. Overall survival and the received treatment were determined. Survival data were analyzed using Kaplan-Meir Survival curves using log rank test and multivariate analysis.

**Results:** For 415 patients, the mean age was 57 years, 317 were males. At presentation, 65.5% were CTP A, 28% were CTP B and 6.5% were CTP C. Most of patients were ALBI grade 2 (63.6%), 25.5% were ALBI grade 2 A while 38.1% were ALBI grade 2B. ALBI grade 1 & 3 were 21.4% & 15% respectively. Patients with CTP A were classified according to ALBI score to 32.7% & 67.3% ALBI grade 1 & 2 respectively and according to PALBI score to 19%, 45.2% and 35.8% PALBI grades 1, 2 & 3 respectively. The overall survival was 22.8 months; the median survival was better in patients with ALBI grade 1 than ALBI 2 & 3 (33.8, 22.1 and 6.8 months respectively, $P < 0.001$). Moreover, the median survival for ALBI grade 2 A patients was better than ALBI 2B (26.3 vs. 16.9 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(undefined (mean 34.7 months), 30.8, 25.5, 10.7, 6.8 and 5.8 months respectively ($P < 0.001$)). On classifying CTP A patients using ALBI and ALBI-T scores, we found that the median survival increased in CTP A patients after further classification by our tested scores, as it was 28.5 months for all CTP A patients, to be 33.8 months in ALBI grade 1 and 34.7 & 30.8 months ALBI-T grade 0 &1 respectively ($P < 0.001$).

**Conclusion:** ALBI score was found to be an independent prognostic factor that classifies patients with HCC according to liver functions better than CTP score. Further sub classification for ALBI grade 2, were found to be significant to identify patients with better liver functions. However, ALBI-T score was found to be the best total prognostic scoring system for predicting survival of patients with HCC that allow more convenient treatment modalities.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0607 ALBI SCORE: BEST PREDICTOR OF SHORT-TERM MORTALITY IN HEPATOCELLULAR CARCINOMA

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**Introduction:** ALBI score is a simple and objective tool to assess liver function in patients with hepatocellular carcinoma (HCC) [1,2].
**Aims & Methods:** Our aim was to compare the ALBI score with Child-Pugh and BCLC scores as a mortality predictor. ALBI score was calculated in HCC patients followed in Hepatology consultation between 2010 and 2015. ALBI score results were stratified as: grade 1 (values $< -2.60$), grade 2 (between $-2.60$; $-1.39$) and grade 3 (values $> -1.39$).
**Results:** A total of 167 HCC patients were included (87% male), with a median age of 65 years (IQR: 19), followed for a median period of 15 months (IQR: 4–28). The median ALBI score was $-3.088$ (IQR: $-0.798$), classified as grade 1 and grade 2 in 77% and 23% cases, respectively. The majority of grade 1 patients were Child-Pugh A (71%) and BCLC stage B (41%). Grade 2 patients were Child-Pugh B (44%) and BCLC stage C (34%). The mortality rates at 6, 12 and 24 months were 68%, 56% and 29%, respectively. The ALBI score showed good ability to predict 6-months mortality (area under the curve [AUROC] of 0.73 IC 95% (0.65–0.81) ($p < 0.001$). Considering, a cut-off value of $-3.847$, this score showed high sensitivity (98%) and specificity (92%) predicting 6-month mortality. At 12 and 24 months, despite preserving the capacity to predict mortality, ALBI score showed lower AUROC values (0.67 IC 95% (0.59–0.76) and 0.61 IC 95% (0.51–0.70), respectively). At 6 months, the ALBI score was superior to Child-Pugh and BCLC classifications (AUROC 0.71 IC 95% (0.62–0.80) vs. 0.68 IC 95% (0.58–0.78) vs. 0.68 IC 95% (0.58–0.77), $p < 0.0001$). However, the BCLC classification was superior to the Child-Pugh and ALBI scores predicting mortality at 12 and 24 months (AUROC 0.67 vs. 0.64 vs. 0.66 and AUROC 0.69 vs. 0.64 vs. 0.62, respectively), $p < 0.001$.
**Conclusion:** ALBI score may be a better predictor of short-term mortality in patients with HCC. BCLC classification was superior predicting long-term mortality.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0608 MARITAL STATUS AND SURVIVAL IN PATIENTS WITH PRIMARY LIVER CANCER: AN ANSWER FROM SEER

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**Introduction:** Primary liver cancer still represents the common cancer and a leading cause of cancer-related death worldwide [1, 2]. The 5-year survival rate for patients with liver cancer is still poor [3]. Marital status, as an important type of social support, has been reported to provide several health benefits for various diseases. Early studies had demonstrated that married persons had greater longevity and overall better health compared with the unmarried (including divorced/separated, widowed and single) [4–6]. Hence, whether marital status is associated with favorable survival among cancer patients has aroused public interest. To our knowledge, no research has reported the relationship between marital status and prognosis of primary liver cancer so far.
**Objective**: Marital status is viewed as an independent prognostic factor for survival in various cancer types. However, its role in primary liver cancer hasn't been thoroughly explored. In this study, we aimed to investigate the impact of marital status on survival outcomes among liver cancer patients.
**Methods:** We used the Surveillance, Epidemiology and End Results (SEER) database to identify 40,809 patients diagnosed with primary liver cancer between 2004 and 2012. Kaplan-Meier analysis and Cox regression were performed to identify the influence of diverse marital status on overall and liver cancer-specific survival.
**Results:** We finally identified 40,809 eligible liver cancer patients between 2004 and 2012, including 21,939 (53.8%) patients were married at diagnosis and 18,870 (46.2%) were unmarried (including the divorced/separated, the widowed, the single). Married patients had better overall and cause-specific survival outcomes compared with patients who were divorced/separated, widowed, single, respectively. The benefit associated with marriage still persisted even after adjusted for known confounders. Widowed individuals were at greater risk of overall and cancer-specific mortality compared to other groups. Similar associations were observed in subgroup analyses according to SEER stage.
**Conclusion:** Results from our study indicated that married persons enjoyed survival benefits and unmarried patients were at higher risk of overall and cancer-specific cancer mortality. We speculated that psychosocial factors and social support may contribute better survival outcomes among cancer patients, especial for the widowed. More social supports and care should be provided for unmarried patients in our clinic practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0609 NON-INVASIVE FIBROSIS SCORES AND LIVER IMAGING IN CHARACTERIZING INCIDENTALLY DETECTED SPACE OCCUPYING LIVER LESIONS IN CHRONIC HEPATITIS C

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**Introduction:** Limited studies describe incidental space occupying lesions (SOL) in liver during pretreatment evaluation in chronic hepatitis C (CHC).
**Aims & Methods:** We aim to evaluate the occurrence and nature of SOL) on liver imaging in patients with chronic hepatitis C (CHC) receiving antiviral therapy (AVT) and the role of combination of non-invasive fibrosis scores in its characterization. 1540 patients (from January 2002 to July 2014) with CHC who underwent ultrasound (USG) scan, liver biopsy (LB) and received conventional (pegylated interferon and ribavirin) dual AVT were retrospectively analyzed for the occurrence and nature of SOL prior to initiation of AVT and thereafter.
**Results:** Mean age of patients was $41.9 \pm 9.7$ years (85% males), predominantly genotype 4 (65%) and genotype 1 (11%). Pretreatment LB showed (Scheuer classification) stage-0 fibrosis (F0) in 1.9%, stage-1 (F1) in 32.9%, stage-2 (F2) in 39.5%, stage-3 (F3) in 19% and stage-4 (F4) in 6.6% patients. Median follow-up was 3.5 years (5390 patient-years). Computed Tomography (CT) and Magnetic resonance imaging (MR) scans were performed in 1185 and 560 patients respectively prior to AVT and during follow up. Of the patients with F4 on LB, USG identified cirrhosis in 68%. Of all the patients reported with cirrhosis on USG, F4 was seen in 16.6% and advanced fibrosis (F3 and F4) in 53.4%. Routine pretreatment USG showed fatty liver in 334 (20.8%). Incidental SOL included, cysts in 21 (1.3%), hemangioma in 41 (2.6%) and hypoechoic lesions in 14 (0.9%). CT and/or MR scan did not change diagnosis in most of these SOL, except in two hypoechoic lesions detected pretreatment (one was confirmed as hepatocellular carcinoma (HCC) by CT and another by MR) and one hypoechoic lesion during post AVT follow up (confirmed as HCC in MR). CT and MR identified three and one HCC respectively that were missed on USG against cirrhotic background. Four patients had HCC during pretreatment evaluation and 11 developed HCC during post AVT follow up. The mean alpha fetoprotein (AFP) at diagnosis of new onset HCC on follow up was $63.3 \pm 1173.8$ (vs $16.2 \pm 118.1$ for non HCC patients, $p = 0.001$). Elevated AFP levels were seen in 81.8% of these patients. Independent pretreatment predictors of new onset HCC were pre-AVT albumin (adjusted odds ratio [AOR]= 0.718, confidence interval [CI] = 0.527–0.979, $p = 0.036$) and GGT (AOR = 1.008, CI = 1.003–1.012, $p = 0.001$). We derived a predicting model, 7.86–0.331 (albumin, g/dL) + 0.007(GGT, IU/L) which at a cut off 5.0 has sensitivity of 85.7% and 78.3% in predicting new-onset HCC.
**Conclusion:** Most of the incidental SOL detected in routine pre-AVT USG retained diagnostic consistency with further radiological imaging with CT and MR. A predicting model including pre-AVT albumin and GGT showed high predictive accuracy for development of HCC during post treatment follow up, This model could be applied as a guide to consider further radiologic evaluation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0610 EVALUATION OF SERUM NITRIC OXIDE LEVEL AND TUMOR EXPRESSION OF INDUCIBLE NITRIC OXIDE SYNTHETASE ENZYME IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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**Introduction:**: HCC is the commonest liver primary tumor. Several studies have evaluated the cost-effectiveness of surveillance for HCC using ultrasonography

**Abstract No: P0611**

**Table 1:** Patient characteristics and annual costs for different Patient groups

| patient group | 1 (n = 20) | 2 (n = 19) | 3 (n = 32) | 4 (n = 15) | 5 (n = 15) | 6 (n = 16) | all (n = 117) |
|---|---|---|---|---|---|---|---|
| **age** | **38.7 ± 12.6** | **34.8 ± 13.0** | **39.0 ± 12.2** | **44.6 ± 12.9** | **54.9 ± 13.1** | **40.3 ± 10.8** | **41.2 ± 13.5** |
| **hospital days** | **0.2 ± 0.8** | **0.1 ± 0.3** | **0.1 ± 0.4** | **0.3 ± 1.0** | **5.2 ± 9.5** | **1.4 ± 3.1** | **0.8 ± 3.9** |
| **treatment** | | | | | | | |
| none | 100.0% | 100.0% | 0.0% | 13.3% | 13.3% | 37.5% | 41.9% |
| only IFN | 0.0% | 0.0% | 3.1% | 6.7% | 0.0% | 18.8% | 4.3% |
| only NUKS | 0.0% | 0.0% | 87.5% | 80.0% | 73.3% | 25.0% | 47.0% |
| IFN+NUKS | 0.0% | 0.0% | 9.4% | 0.0% | 13.3% | 18.8% | 6.8% |
| **ambulatory care** | **€ 225** | **€ 199** | **€ 427** | **€ 428** | **€ 489** | **€ 586** | **€ 385** |
| doctor fees | € 30 | € 23 | € 68 | € 61 | € 74 | € 64 | € 54 |
| general lab tests | € 62 | € 47 | € 83 | € 76 | € 82 | € 70 | € 71 |
| virological tests | € 96 | € 97 | € 246 | € 247 | € 272 | € 389 | € 219 |
| imaging | € 37 | € 32 | € 31 | € 43 | € 62 | € 62 | € 42 |
| **pharmaceuticals** | **€ 0** | **€ 0** | **€ 5.174** | **€ 4.990** | **€ 4.604** | **€ 2.631** | **€ 3.005** |
| antiviral treatment | € 0 | € 0 | € 5.174 | € 4.952 | € 4.510 | € 2.607 | € 2.985 |
| co-medication | € 0 | € 0 | € 0 | € 37 | € 94 | € 25 | € 20 |
| **inpatient care** | **€ 29** | **€ 22** | **€ 17** | **€ 39** | **€ 515** | **€ 249** | **€ 118** |
| **total costs** | **€ 255** | **€ 221** | **€ 5.618** | **€ 5.457** | **€ 5.609** | **€ 3.466** | **€ 3.509** |

and AFP. NO is a product of the conversion of L-arginine to L-citrulline by NOS. iNOS is a class of NOS enzymes that produces much larger amounts of NO and has been detected in many human tumors.

**Aims & Methods:** To evaluate serum NO levels and tumor expression of iNOS in HCC patients. Subjects and Methods: Group (1) 50 patients with liver cirrhosis and HCC. Group (2) 25 patients with liver cirrhosis without HCC. Group (3) 10 normal individuals. History taking, clinical examination and Laboratory investigations (complete liver profile, AFP, NO) were done. Tumor and corresponding peri-tumor iNOS expressions were measured using Immuno-histo-chemistry technique.

**Results:** The median level of nitric oxide was significantly higher in Group (1) than in other two groups with a diagnostic sensitivity of (56%) and specificity of (80%) at a cut-off level of 58.5 $\mu$mol/l. combined usage of both AFP and NO raised the diagnostic sensitivity for HCC up to 64%. The level of tumoral iNOS was significantly higher than peri-tumoral iNOS in overall samples. The level of tumoral iNOS was significantly lower in low grade (I) HCC smears than in high grades (II& III) smears. There was significant positive correlation between serum NO and both tumor iNOS and tumor size.

**Conclusion:** NO can be considered as a novel diagnostic marker for HCC and the simultaneous determination of NO and AFP gave significant improvement in HCC detection. Its significant positive correlation with tumor iNOS suggests that the elevated tumor expression of iNOS is the source for the increased serum levels of NO in these patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0611 HBV-INFECTION IN GERMANY – COSTS IN A REAL-LIFE SETTING

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**Introduction:** An estimated 500,000 individuals are infected with HBV in Germany but medical costs caused by HBV-infection are not known. In particular costs for diagnosis and monitoring of hepatitis B in different phases of the dynamic disease from chronic hepatitis up to the cirrhotic state and the amount of pharmaceutical costs are not defined. The introduction of nucleos(t) ides (NUC) has replaced treatment with interferons (IFN) which was associated with severe side-effects.

**Aims & Methods:** The aim of the study was to assess the direct medical costs of treating HBV-infection in a real-life setting. Data on resource utilisation of 117 HBV-infected patients was obtained from an outpatient clinic at a tertiary referral center. Patients were categorised in six groups: (1.) low viraemic carriers, (2.) high viraemic carriers, (3.) chronic hepatitis B, (4.) chronic hepatitis B with compensated cirrhosis, (5.) chronic hepatitis B with decompensated cirrhosis, (6.) chronic hepatitis B/D co-infection. Ambulatory care which comprises basic diagnostic procedures and monitoring was categorised in doctor fees, general lab tests, virological diagnostics as well as imaging. Ambulatory costs are based on the German remuneration scheme for outpatient services (EBM). Pharmaceutical costs were derived from German drug directory (Lauer-Taxe). Inpatient care costs were calculated based on German Diagnosis Related Group (g-DRG) listings. The investigation period covered 3.5 years from 07/2009 to 12/2012.

**Results:** Patient characteristics and annual treatment costs of the different groups are shown in **Table 1**. 47% (55 patients) received NUCs, 4.3% (5 patients) IFN only and 6.8% (8 patients) were treated with IFN and NUCs during the study period. Total treatment costs ranged between €221 and €5,609 per year in different patient groups. Low and high viraemic carrier patients caused average annual costs of about €250. Patient groups 3–6 had mean total costs between €3,466 and €5,618 per year predominantly due to antiviral treatment costs. Medications for the treatment of HBV-associated symptoms were of minor importance. Hospitalisation was rare, except in patients with decompensated cirrhosis and with hepatitis D-coinfection.

**Conclusion:** Management of chronic hepatitis B-infection is expensive. Antiviral therapy accounts for the majority of costs. Real-life costs are lower compared to estimated guideline-based treatment costs [1]. Only a quarter of the infected patients are diagnosed and about a quarter of the diagnosed are treated. Nevertheless the economic burden of the disease is high.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0612 KLEBSIELLA PNEUMONIAE INDUCED PYOGENIC LIVER ABSCESS IN CRITICALLY ILL PATIENTS: A RETROSPECTIVE STUDY FROM A CHINESE MEDICAL CENTER, 1994–2015

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**Introduction:** Klebsiella pneumoniae-induced pyogenic liver abscess (KP-PLA) mainly occurs in the *Asia-Pacific* region. However, there were only few studies came from mainland China and none of which highlighted critically ill patients. Moreover, the clinical presentation and prognosis of critically ill patients with KP-PLA or invasive KP-PLA syndrome remain unclear.

**Aims & Methods:** The aim of this study was hence to investigate the clinical characteristics of KP-PLA with a focus on critically ill patients in mainland China by retrospective review of medical records in a tertiary teaching hospital. We performed a retrospective analysis of consecutive PLA cases by accessing ICD-9 codes (572.0) of the hospital discharge database from May 1994 to April 2013 and ICD-10 codes (k75.0) from May 2013 to December 2015 at a 2400-bed tertiary teaching hospital in mainland China. We only enrolled critically ill patients with PLA admitted to Intensive Care Units (ICU) during hospitalization and collected the Acute Physiology and Chronic Health Evaluation II (APACHE II) score within 24 hours after transferring to ICU. The pathogenic bacteria isolated from blood and pus were identified and susceptibility testing was performed afterwards. Patient data such as demographics, underlying diseases, clinical features, microbiological findings and clinical outcomes were documented and analyzed.

**Results:** Ninety-seven out of 802 PLA patients were admitted to ICU and were included in this study. Compared with the initial 10 years, there was no significant change in the proportion of PLA patients that became critically ill in recent years (2004–2015) – (12.3% vs. 10.9%, p = 0.681). 43 patients (44.3%) developed septic shock, and 18 patients (18.6%) died eventually. *Klebsiella pneumoniae* (KP) was identified in 72.3% (n = 47) of the culture-positive PLA patients (n = 65), of

which 2 strains showed extended-spectrum beta-lactamases (ESBL) production. KP-PLA was predominately community-acquired (55.3% vs. 16.7%, $p = 0.005$) and less commonly occurred in patients who previously had been diagnosed with cancer (10.6% vs. 44.4%, $p = 0.005$) or underwent hepatobiliary surgery (27.7% vs. 77.8%, $p < 0.001$), as compared with non-KP-PLA. Nine cases of KP-PLA patients (19.1%) developed invasive KP-PLA syndrome with metastatic infection at distant sites, including meningitis ($n = 2$), brain abscess ($n = 1$), lung abscess ($n = 1$), pneumonia ($n = 3$) and other infections ($n = 2$), of which 4 patients died ultimately. Patients with invasive KP-PLA syndrome had higher APACHE II score ($21.9 \pm 6.9$ vs. $14.9 \pm 6.6$, $p = 0.016$.), longer length of hospitalization ($11.7 \pm 10.3$ vs. $8.4 \pm 13.1$, $p = 0.040$) and higher in-hospital mortality (44.4% vs. 18.4%) than patients with non-metastatic KP-PLA.
**Conclusion:** KP-PLA is an emerging infectious disease in mainland China. Even with improved early diagnostic techniques and advanced multidisciplinary management over past 2 decades, there were a substantial number of KP-PLA patients that required ICU support. Patients with invasive KP-PLA syndrome had a more severe disease course with higher mortality. Detection of KP-PLA and its catastrophic metastatic complications in critically ill patients deserve more attention.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0613 CHANGING HAV IMMUNITY IN ADULTS OF IRAN: NEW EVIDENCE FOR NEW POLICY

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**Introduction:** Sanitation specially access to safe drinking water is one of the major determinants of hepatitis A (HAV) infection in communities. Iran as a transitional economy has witnessed dramatic improvement in access to safe water and in improvement of sanitation. Previous studies from Iran about two decades ago revealed high level of immunity as early as age 16 years. This study was designed to see the current state of HAV infection in one of the major cities of Iran.
**Aims & Methods:** To determine the age-specific prevalence of immunity to HAV in adults in a major metroplitan of Iran, through a multi stage cluster randomized population based sampling in Shiraz (capital city of Fars province in south of the Iran) among adults $\geq$18 years old were invited to participate. After filling a questionnaire on demographic features, a serum sample for total anti HAV immunoglobulin was taken. The sample size was estimated 500 to cover all neighborhoods of Shiraz, but to be sure about the appropriate number 1000 of inhabitants were invited. Data were analyzed in SPSS software.
**Results:** Of 1000 invitees, 820 participated in this study (response rate 82%) and their mean of age was: $43 \pm 14$ years. 479(58.4%) were female compared to 340(41.5%) who were male. We found that overall immunity against HAV was as $289/820 = 35.2\%$ and HAV immunity was 21.9% in 18–25yrs,31.9% in 26–35yrs, 39.3% in 36–45yrs, 41.4% in 46 55yrs and 30.2% in 56–65yrs age groups. It was also concluded that only age was positively correlated with HAV-Ab immunity (OR = 1.2, 95% CI = 1–1.4, $P < 0.05$) while gender, level of education and co-morbidities did not show any correlation.
**Conclusion:** Epidemiology of HAV has changed in Iran and now HAV vaccination should be a consideration. Further studies to determine the most appropriate age and most appropriate groups to receive this vaccine is warranted
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0614 ASYMPTOMATIC ELEVATION OF AMINOTRANSFERASES IN MILITARY VOLUNTEERS: THE SILENT ROLE OF NAFLD IN A "HEALTHY" POPULATION

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**Introduction:** The use of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in the detection and monitoring of chronic liver disease (CLD) is well established. In the absence of factors such as alcohol consumption or viral infections, the prevalence of non-alcoholic fatty liver disease (NAFLD) and its potential to progress to CLD have gradually been recognized.
**Aims & Methods:** Our aim was to determine the prevalence and etiology of elevated ALT and AST in a sample of military volunteers without known history of liver disease and to correlate ALT elevation with clinical and laboratory parameters associated to the diagnosis of metabolic syndrome and NAFLD. 229 military volunteers were prospectively analyzed. Intervention included a standardized lifestyle assessment questionnaire (comprising present health conditions, family history of liver disease and personal consumption of potentially hepatotoxic substances, namely alcohol, drugs and natural products), collection of biometric parameters (height, weight, waist circumference and blood pressure) and analysis of serum biochemical parameters (general liver disease biomarkers and viral hepatitis serologic tests). The considered variables were statistically correlated to categorized ALT levels (normal $\leq$40 IU/L, normal-high 41–55 IU/L and elevated $>$55 IU/L).
**Results:** From the 229 analyzed volunteers, 205 (89.5%) were males. Given the major gender disproportion, only male individuals were considered for statistical analysis. ALT or AST elevation was present in 18.7% and 28.3% of individuals, respectively, whereas 15.8% showed normal-high levels of ALT. In our sample, 17.6% of individuals had elevated body mass index, 19.5% increased waist circumference and 39.5% hypertension. 59.3% of male volunteers showed elevated total cholesterol, 10.3% HDL-cholesterol, 27.3% elevated triglycerides and 8.5% increased fasting glucose. Categorized ALT levels correlated with body mass index ($p < 0.001$), waist circumference ($p < 0.001$), blood pressure ($p < 0.01$), serum triglyceride levels ($p < 0.001$) and serum total cholesterol levels ($p < 0.01$). No correlation was identified between categorized ALT levels and serum HDL-cholesterol or glucose levels. Furthermore, normal ALT levels were associated to normal body mass index, waist circumference, blood pressure, triglycerides and total cholesterol levels. On the other hand, elevated ALT was associated to obesity, increased waist circumference and hypercholesterolemia. More than half the individuals with ALT elevation had no apparent cause for this elevation.
**Conclusion:** Elevated ALT was common in our sample of military volunteers without known history of liver disease and, in the majority of cases, was associated to metabolic syndrome and NAFLD risk factors, such as obesity and dyslipidemia.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0615 IDENTIFICATION OF PALLIATIVE CARE NEEDS IN HEPATOLOGY – EXPERIENCE OF A MAJOR REFERRAL CENTRE

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**Introduction:** Chronic liver disease is a major cause of morbidity and mortality that affects active adults of working age. Palliative care policies are not clearly established in chronic liver disease. The NECPAL CCOMS-ICO© is a tool to identify palliative care needs, including in liver disease.
**Aims & Methods:** This prospective single-centre prospective observational study aimed at identifying palliative care needs in hospitalized liver patients in a tertiary Liver Unit. The NECPAL CCOMS-ICO© was applied to all hospitalized patients admitted from 1st August to 30th September 2015.
**Results:** Forty-six patients (80.4 male) with chronic liver disease were included with a median age of 60 years (SD 10.7). Alcoholic abuse was the most prevalent etiology (76%). 47% had a MELD score greater than 15. Using NECPAL tool, 89% of the patients were considered as requiring some type of palliative intervention. Those needs were subjectively identified by clinicians in only 58.6% of the cases. Caregiver perception of palliative care needs was even lower (13%). 14% of the patients were admitted in intensive care unit, all of them considered as needing palliative care by NECPAL. Mortality rate was 21.7%, 40% due to hepatocellular carcinoma. All deaths occurred in patients with MELD score superior to 15.
**Conclusion:** Clinicians and caregivers were not aware of palliative care needs. End of life care needs must be promptly identified and provided, in order to improve quality of life of terminal patients. The NECPAL CCOMS-ICO© represents a feasible and easy to use tool to identify patients in need of palliative care in chronic liver disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0616 UNDER-REPORTING OF COMPLEMENTARY AND ALTERNATIVE DRUG USE IN LIVER DISEASE PATIENTS

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**Introduction:** Complementary and alternative medicine (CAM) encompasses a huge variety of treatments including homeopathy, herbal medications and acupuncture. We hypothesize that CAM use in liver disease patients is underreported in clinical practice and can lead to relevant pharmacological interactions.
**Aims & Methods:** The aims of this study were to assess the prevalence and type of CAM use, and experiences with CAM use in liver disease patients. We

conducted a cross-sectional survey among the members of the Dutch Liver Patients Association. All members received a questionnaire through Survey Monkey©. The questionnaire included 26 questions about demographics, liver disease, frequency, type, and experiences with CAM use. Results are presented as mean, standard deviation (SD), and frequencies.
**Results:** We received 210 completed questionnaires. Mean age of respondents was 55 years (SD 13.5), 62 (30%) respondents were male and main liver diseases were primary sclerosing cholangitis (n = 50, 24%), primary biliary cholangitis (n = 40, 19%), autoimmune hepatitis (n = 40, 19%), and viral hepatitis (n = 16, 8%). A total of 96 (43%) patients reported CAM use; type of CAM was diverse and silymarin was most frequently reported (n = 16). Up to 35% of CAM users had not divulged CAM use to their physician. The majority of patients (n = 63, 76%) experienced beneficial effects of CAM and 58 patients (71%) would recommend CAM to other patients.
**Conclusion:** Prevalence of CAM use is high (43%) in liver disease patients and 35% of patients do not report CAM use to their physician. Clarity about CAM use can prevent potential harmful interactions with prescribed medication. Physicians should actively ask for CAM use.
**Disclosure of Interest:** J.P.H. Drenth: Prof. Dr. Drenth reports other from Gilead, grants and other from Janssen, other from BMS, grants and other from AbbVie, grants from dr. Falk, grants from Ipsen, grants from Novartis, grants from Zambon, from Merck, outside the submitted work
All other authors have declared no conflicts of interest.

## P0617 INCIDENCE AND PREDICTORS OF HEPATITIS C TREATMENT INITIATION AMONG PEOPLE WHO INJECT DRUGS: LONGITUDINAL DATA FROM A GREEK TERTIARY CENTER, 2009–2015

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**Introduction:** People who inject drugs (PWID) account for a large burden of hepatitis C virus (HCV) infection. However, they often face several barriers to accessing antiviral treatment. In the era of highly-efficacious direct-acting antivirals (DAAs), knowledge of factors that prevent treatment among PWID is very crucial.
**Aims & Methods:** We retrospectively reviewed consecutive HCV-viraemic PWID visiting a tertiary liver center (January 2009–June 2015). Patients attending a substitution program were managed by a multidisciplinary approach. Kaplan-Meier and Cox regression analyses were used to evaluate treatment initiation and its correlates.
**Results:** A total of 177 PWID (141 males, 41.7 ± 10.6 years, 19.7% cirrhotics, 77.9% treatment-naïve) were included: 74 (41.8%) former drug users, 88 (49.7%) attending substitution programs and 15 (8.5%) active users. Treatment was initiated in 101 (57.1%), with the vast majority (91.1%) receiving peginterferon/ribavirin(PR). The cumulative probability of treatment was 61.8% over 3 years. During the DAA era treatment was prescribed to 15 out of 35 who visited the center. DAAs were prescribed in 9 patients; only 5 cases in an all-oral regimen. There was no impact of calendar time (2009–11 vs 2012–13 vs 2014–15) on treatment initiation incidence (RR: 1.02, 95%CI: 0.78–1.32; P = 0.88). Compared to former drug users, active users were less likely to initiate treatment (RR: 0.17, 95%CI: 0.03–0.91; P = 0.04), whereas no difference was observed for patients under substitution (RR: 0.60, 95%CI: 0.30–1.18; P = 0.14). ALT < 40 IU/L (RR: 0.23, 95%CI: 0.09–0.6; P = 0.002), genotype 1–4 (RR:0.36, 95%CI: 0.17–0.73; P = 0.005) and comorbidities that constitute contraindications to interferon (RR: 0.36, 95%CI: 0.19–0.69; P = 0.002) were inversely related to treatment initiation.
**Conclusion:** In PWID with HCV infection, active drug use and drawbacks pertinent to PR therapy posed significant barriers to treatment. Few PWIDs had been referred and initiated DAAs during 2014–15. In the era of financial crisis delineating the barriers to initiate DDAs should urgently be explored in order to reduce the burden of the disease in this population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0618 ENDOSCOPIC TREATMENT OF BILIARY STRICTURES FOLLOWING LIVER TRANSPLANTATION- 15 YEARS' EXPERIENCE IN A TERTIARY TRANSPLANT CENTER

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**Introduction:** Biliary strictures are a common complication of liver transplantation. The standard treatment is repeated ERCP with placement of increasing numbers of plastic stents. Despite high success rates, some strictures fail to resolve and require surgery as definitive treatment.
**Aims & Methods:** We aimed to find predictors for failure of endoscopic treatment in order to avoid unnecessary procedures in patients who have low probability of recovery under standard treatment. Database of Gastroenterology Department at Tel Aviv Medical Center was retrospectively reviewed, and data regarding patients who underwent liver transplantation and developed biliary strictures was analyzed.
**Results:** 31 patients met the study criteria. 24 (77.4%) resolved with endoscopic treatment and 7 ultimately required surgery. There were no significant differences between stent responders and non-responders regarding demographics, transplant and postoperative hospitalization data, time from transplantation to presentation with stricture, total number of ERCP sessions or maximal number of stents. A significant difference was noted in the time elapsed between the first and the second ERCP, whereby ERCP non-responders required a second urgent procedure sooner than responders (0.99 ± 1 vs. 2.17 ± 1.39 months, p = 0.046). Patients presenting electively had a 95% endoscopic success rate, while those presenting urgently had a 55% failure rate (p = 0.004).
**Conclusion:** This study identified urgent repeat ERCP as a harbinger of ultimate failure of plastic stent treatment for biliary stricture following liver transplant. This finding may assist earlier triage of these patients toward alternative treatment such as metal stents or surgery, thus sparing needless procedures and complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0619 EFFICACY AND SAFETY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN ELDERLY PATIENTS WITH CHOLEDOCHOLITHIASIS

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**Introduction:** Choledocholithiasis is a frequent condition in the elderly. Therapeutic Endoscopic Retrograde Cholangiopancreatography (ERCP) in the elderly patients is increasing as a result of the population ageing.
**Aims & Methods:** To evaluate the efficacy and safety of therapeutic ERCP in the elderly. A retrospective study which included patients with choledocholithiasis who underwent therapeutic ERCP during a 6-year period (2009–2015). The patients were divided in two groups: age ≥75 years and age <75 years. Variables analyzed: gender, antiplatelets/antithrombotic drugs, American Society of Anesthesiologists (ASA) classification, periampullary duodenal diverticulum, diameter of the common bile duct, number of the common bile duct stones, diameter of the larger stone, complete/incomplete common bile duct stone removal, placement of biliary stent and early complications (<30 days): pancreatitis, bleeding, cholangitis, hepatic abscess and death.
**Results:** Two hundred twenty-nine patients were included: 133 female, 123 patients with age ≥75 years. The patients who were ≥75 years were more frequently on antiplatelet drugs (30% vs 22%, p = 0.001) and on antithrombotic drugs (14% vs 6%, p = 0.041), had more commonly an ASA classification >2 (99% vs 90%, p < 0.001), had more frequently a periampullary diverticulum (36% vs 21%, p = 0.012) and presented a higher mean diameter of the common bile duct (14 mm vs 12 mm, p < 0.001) and a higher mean diameter of the larger stone (12 mm vs 10 mm, p < 0.001). The proportion of patients with multiple common bile duct stones was not significantly higher in this group (63% vs 57%, p = 0.294). The rate of complete common bile duct stone removal and of biliary stent placement was similar in the two groups (80% vs 88%, p = 0.137; 20% vs 12%, p = 0.102, respectively). Moreover, there was no significant difference between the two groups regarding overall complications (15% vs 12%, p = 0.601), pancreatitis (4% vs 5%, p = 0.530), bleeding (4% vs 5%, p = 0.530), cholangitis (2% vs 2%, p = 0.570), hepatic abscess (2% vs 0.2%, p = 0.501) and death (0% vs 2%, p = 0.213).
**Conclusion:** Therapeutic ERCP is an effective procedure in the elderly patients with choledocholithiasis. The occurrence of complications is not increased in these patients, although antiplatelet/antithrombotic drugs are more commonly used and their ASA classification is higher. As such, ERCP is a valid therapeutic procedure in the elderly patients with choledocholithiasis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0620 COST IMPACT OF LONG-TERM HEALTH CARE CONSUMPTION AND SICK LEAVE IN PATIENTS WITH PERSISTENT ABDOMINAL PAIN AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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**Introduction:** In the Netherlands, annually 23,000 cholecystectomies are performed against hospital-related costs of 55 million euro.[1] Remarkably, gallbladder removal appears to be ineffective in terms of pain relief, in up to 40% of patients with uncomplicated symptomatic cholecystolithiasis.[2] Although several studies report persistent abdominal pain after cholecystectomy, there is no literature on the actual burden of this pain to the health care system.
**Aims & Methods:** Aim: To determine health care consumption and the related costs in patients with persistent abdominal pain after cholecystectomy. Methods: A prospective multicentre cohort study included patients with uncomplicated symptomatic cholecystolithiasis who had a cholecystectomy between June 2012 and June 2014. Persistent postoperative abdominal pain was reported by 146 of the surveyed 360 patients (40.6%) at 24 weeks after surgery.[2] For these patients health care consumption was assessed in February 2016 using Patients' Experience of Surgery Questionnaire (PESQ), Medical Consumption Questionnaire (iMCQ) and patients' medical records. Sick leave and productivity loss of (un) paid work were assessed using Productivity Cost Questionnaire (iPCQ). Health care consumption was defined as home, primary and secondary care consultations, emergency department and hospital admissions, and medication use. Related costs were calculated according the Dutch "Guideline for performing economic evaluations in health care", using Euro 2014 prices.
**Results:** Complete assessment of health care use was obtained from 124/146 patients (85%). Sixty-nine patients (55.6%) had additional care for persistent abdominal pain after cholecystectomy; 38 patients (30.6%) received primary care with an average number of 3 (SD 2.4) visits, 46 patients (37.1%) received secondary care with an average number of 4.7 (SD 4.5) visits, 20 patients (16%) were admitted in the emergency department, and 11 patients (8.9%) were admitted in the hospital. Forty-two patients (33.9%) had additional diagnostic procedures, which revealed gallstone or surgery related causes in six patients. As treatment, 22 patients (17.7%) reported use of medication; 13 (10%) used analgesia and 12 (9.6%) used proton pump inhibitors. Seven patients (5.6%) needed other additional treatments, of which 3 had an Endoscopic Retrograde CholangioPancreatography with stone extraction. The estimated mean medical costs (excl. medication) for persistent abdominal pain since cholecystectomy were €1239 (SD €3573) per patient. The estimated mean costs of sick leave and productivity loss of paid and unpaid work due to persistent abdominal pain since cholecystectomy were €727 (SD €2163) per patient.
**Conclusion:** Fifty-five percent of patients needed additional care for persistent abdominal pain after cholecystectomy. Optimized indication for cholecystectomy will reduce postoperative pain for patients and partly reduce costs after cholecystectomy for health care system and employers. The gain is that less money is spent on unnecessary surgery, but patients will use other resources as therapy for their symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0621 A MEASURE OF QUALITY IN MANAGEMENT OF GALL BLADDER POLYPS IN A DISTRICT GENERAL HOSPITAL: THE UNITED KINGDOM EXPERIENCE

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**Introduction:** Lesions projecting from the gall bladder wall into the gall bladder are called gall bladder polyps. It is usually an incidental diagnosis. Most gall bladder polyps are benign but may be malignant in some cases, therefore an early detection and appropriate treatment of these is required. There are two categories of gall bladder polyps: 1) Benign polyps like cholesterol deposits, inflammatory polyps and epithelial tumours like adenomas or mesenchyma tumours like fibromas, lipomas, haemangiomas etc 2) Malignant polyps like gall blabber carcinoma. It has been suggested that age more than 50 years, presence of Diabetes Mellitus, polyp size more than 1.5 cms specially in solitary sessile hypoehogenic lesions and presence of pain make high risk for polyps to be malignant. However there are no clear guidelines on their management. Pragmatically polyps less than 1 cm in size and asymptomatic are monitored with an ultrasound after 6–12 months. However other studies have suggested that diameter alone is not a safe exclusion criteria and cholecystectomy should be considered for any polyp more than 6 mm in size. This study aims to measure quality in management of gall bladder polyps in a sample district hospital in the United Kingdom. It is in turn dependent upon quality of radiological reporting
**Aims & Methods:** It is a retrospective study. To measure quality of radiological reporting of gall bladder polyps, a check list was devised to see if a) Full description of characteristics of polyps was described. b) Whether it had been documented if patient was symptomatic or not and thus achieved a clinical correlation and c) Polyps more than 6 mm size were monitored bi-annually
**Results:** All patients with a diagnosis of gall bladder polyp in a sample district general hospital of United Kingdom over a period of six months in 2015 were identified through IT records. A total of 34 Patients were studied all of whom had an ultrasound of the abdomen. 27 patients were above 50 years of age while 7 were below 50 years. Only 4 patients were male and 30 were females. The polyp characteristics were fully described in all radiological reports. All reports had indication described by the doctor indicating presence or absence of symptoms. It was not documented whether they had diabetes or not in any patient. Upon further investigations it transpired that 8 patients were not diabetic and in another 06 it could not be determined if they were diabetic, while 20 patients had diabetes mellitus. Regarding monitoring, in 06 patients solitary polyps were found and they were more than 1.5 cm in size. All these patients were referred for surgical opinion. Repeat US scan was arranged in six months' time. Only 02 of them showed progression and had laparoscopic cholecystectomy. Another 23 patients had their repeat ultrasound in 12 months and did not show any progression. All of them had multiple polyps ranging between 0.5 mm to 15 mm. 01 patient had multiple polyps ranging between 0.3 mm-10mm but following first scan no follow up had been arranged. None of the patients had CT, MRCP or EUS as these were not required
**Conclusion:** This study has shown that despite no clear guidelines on management of gall bladder polyp, in a sample district general hospital of United Kingdom, a reasonable pragmatic management plan was being undertaken as a measure of quality. Overall appropriate reporting is undertaken by the radiologists, follow up scans are arranged for patients found to have gall bladder polyps and adequate referrals to surgeons for laparoscopic cholecystectomy are made. However importance of Diabetes Mellitus in this group of patients is being less emphasised. Further studies should be undertaken to see if following the surgery, histology is being checked and documented to have been seen. Also how frequently if at all cancer is picked up in these post-operative samples. Experts in hepato-biliary disease need to provide guidelines to the general hospitals on gall bladder polyp cancer risk stratification. There shall then be clear goals in quality for general hospital to aspire to in management of gall bladder polyps
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0622 THE DIAGNOSTIC PERFORMANCE OF NON-INVASIVE FIBROSIS MARKERS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND PRIMARY BILIARY CHOLANGITIS AND AUTOIMMUNE HEPATITIS VARIANT FORM: IS THERE ANY DIFFERENCE?

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**Introduction:** The pathogenesis of primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH) variant form remains poorly understood and it is debated whether this syndrome represents a distinct entity or a variant of PBC or AIH [1]. To the best of our knowledge, there is no published data on the diagnostic performance of non-invasive fibrosis markers in this group of patients.
**Aims & Methods:** The aim of the study was to evaluate and compare the ability of non-invasive fibrosis markers for staging of liver fibrosis in patients with PBC and PBC-AIH variant form, thereby determining the viability of grouping these patients together for the analysis. Ninety-two patients with PBC and 45 patients with PBC-AIH variant form were enrolled in the study and analyzed for the following parameters of liver fibrosis: Fibrosis 4 score (FIB-4), aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR), AST to platelet count ratio (APRI), and platelet count to spleen diameter (PC/SD) ratio. The diagnosis of PBC-AIH variant form was based on the "Paris criteria" [2]. All PBC patients were treated with ursodeoxycholic acid (UDCA), and all patients with PBC-AIH variant form received a combination of UDCA and prednisolone. The diagnostic value of each parameter was evaluated by the area under the receiver operating characteristic curve (AUROC). The AUROCs and standard errors (SE) of non-invasive fibrosis markers in PBC and PBC-AIH patients were compared using Z-statistic.
**Results:** Among the 92 PBC patients (median age [25th – 75th interquartile range] 54 years [49–62]; 92.6% were female), 48 (50.5%) had significant fibrosis (≥F2), 37 (39%) had severe fibrosis (≥F3), and 20 (21.1%) had cirrhosis (F4). In PBC-AIH group (n = 45; median age 50 years [43.5–57]; 93.3% were female) 34 patients (75.6%) had significant fibrosis (≥F2), 27 (60%) had severe fibrosis (≥F3), and 13 (28.9%) had cirrhosis (F4). The AUROCs of the PC/SD ratio, FIB-4, AAR, and APRI were 0.775, 0.686, 0.639, and 0.608 in PBC and 0.711, 0.722, 0.600, and 0.703 in PBC-AIH variant form, respectively, for significant fibrosis (≥F2); 0.776, 0.694, 0.642, and 0.705 in PBC and 0.802, 0.817, 0.699, and 0.780 in PBC-AIH variant form, respectively, for severe fibrosis (≥F3); and 0.806, 0.715, 0.675, and 0.700 in PBC and 0.866, 0.756, 0.626, and 0.705 in PBC-AIH variant form, respectively, for cirrhosis (F4). There were no significant differences in AUROCs of AAR, APRI, FIB-4, or the PC/SD ratio for the prediction of fibrosis ≥F2, ≥F3, or F4 between the PBC and PBC-AIH groups (Table). However, the AUROCs of FIB-4 and the PC/SD ratio tended to be higher in patients with PBC-AIH variant form.

**Table:** Areas under the receiver operating characteristic curves of AAR, APRI, FIB-4, and PC/SD ratio for the prediction of significant fibrosis (≥F2), severe fibrosis (≥F3), or cirrhosis (F4) in PBC patients and patients with PBC-AIH variant form

| Index | Fibrosis category | AUROC (SE) in patients with PBC (n = 92) | AUROC (SE) in patients with PBC-AIH variant form (n = 45) | Z-statistic | p |
|---|---|---|---|---|---|
| AAR | ≥F2 | 0.662 (0.057) | 0.600 (0.086) | 0.601 | 0.548 |
| | ≥F3 | 0.671 (0.060) | 0.699 (0.080) | −0.280 | 0.779 |
| | F4 | 0.673 (0.073) | 0.626 (0.089) | 0.408 | 0.681 |
| APRI | ≥F2 | 0.708 (0.054) | 0.703 (0.088) | 0.048 | 0.961 |
| | ≥F3 | 0.713 (0.055) | 0.780 (0.068) | −0.766 | 0.440 |
| | F4 | 0.715 (0.062) | 0.705 (0.078) | 0.100 | 0.920 |
| FIB-4 | ≥F2 | 0.693 (0.054) | 0.722 (0.075) | −0.314 | 0.753 |
| | ≥F3 | 0.702 (0.056) | 0.817 (0.066) | −1.329 | 0.181 |
| | F4 | 0.729 (0.063) | 0.756 (0.071) | −0.284 | 0.776 |
| PC/SD ratio | ≥F2 | 0.775 (0.050) | 0.711 (0.092) | 0.611 | 0.548 |
| | ≥F3 | 0.776 (0.051) | 0.802 (0.069) | −0.303 | 0.762 |
| | F4 | 0.806 (0.055) | 0.866 (0.055) | −0.711 | 0.441 |

**Conclusion:** The diagnostic performance of non-invasive fibrosis markers for the diagnosis of fibrosis ≥F2, ≥F3, or F4 did not differ significantly between patients with PBC and PBC-AIH variant form. According to our data, patients with PBC and PBC-AIH variant form may be grouped together for the analysis of the diagnostic performance of non-invasive fibrosis markers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0623 PRIMARY CLOSURE VERSUS T-TUBE AFTER LAPAROSCOPIC COMMON BILE DUCT EXPLORATION FOR CHOLEDOCHOLITHIASIS? A SINGLE CENTER EXPERIENCE


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**Introduction:** Common bile duct exploration (**CBDE**) has the advantage of managing cholecysto- choledocholithiasis by single-stage procedure **(1,2).** There is still a debate about the benefits and drawbacks after t tube usage. The aim of this study is to evaluate the value of primary common bile duct **(CBD)** closure and routine T-tube usage after laparoscopic **CBDE**.
**Aims & Methods:** One hundred ninety two patients underwent laparoscopic **CBDE** by choledochotomy for **CBD** stones. Patients were divided into two Groups. **Group (A):** 55 patients were managed by primary closure of the **CBD**, **group (B):** 137 patients were managed by using T-tube after assumed **CBD** clearance. Demographics, pre-operative radiology, intraoperative findings, and post-operative complications were collected and analyzed between the two Groups
**Results:** There was no statistically significant reduction in the serum bilirubin level in the first postoperative day (POD1) with the use of T-tube between the two Groups: 1.2 (0.9–24 mg/dl) and 2 (0.5–27.2 mg/dl) ($P > 0.223$) in Group (A) and (B) respectively. Also in the third post-operative day (POD3) which was 0.9(0.9–18 mg/dl) and 1.1(0.5–14.5 mg/dl) ($P > 0.154$) in Group (A) and (B) respectively. Wound infection and abdominal collections were significantly more obvious in Group **(B)** patients, **($p < 0.003$)** and **($p < 0.002$)** respectively**.** There was no statistically significant difference in bile leakage between both groups as it was encountered in one patient (1.8%) in Group **(A)** and 4 patients (2.9%) in Group **(B), ($p = 0.066$)**. Residual stones were encountered in 10 patients (5.2%); two patients in group A (3.6%) and eight patients in group B (5.8%). Hospital stay was significantly longer in Group **(B)** patients, 4(3–35 days) versus 3(1–13 days) in group (A) **($p < 0.001$).**

| Variable | Group (A) Primary closure(n = 55) | Group (B) T-tube (n = 137) | P value |
|---|---|---|---|
| **(POD1) Total Bilirubin level on first day** | 1.2(0.9–24) | 2(0.5–27.2) | 0.223 |
| **(POD3) Total bilirubin level on third day** | 0.9(0.9–18) | 1.1(0.5–14.5) | 0.154 |
| **Drain removal (days)** | 1 (1–13) | 2 (2–35) | 0.001 |
| **Hospital stay (days)** | 3 (1–13) | 4 (3–35) | 0.001 |
| **Complications*Clavien-Dindo Classification** | 5 (9%) | 19 (14%) | 0.032 |
| **I** | 1 (2%) | 6 (4%) | 0.008 |
| **II** | 0 (0%) | 1 (0.7%) | 0.032 |
| **IIIA** | 0 (0%) | 1 (0.7%) | 0.032 |
| **IIIB** | 4 (7%) | 11 (8%) | 0.032 |
| **Wound infection** | 0 (0%) | 5 (4%) | 0.004 |
| **Bed side management** | | 4 (3%) | |
| **Surgical management** | | 1 (0.7%) | |
| **Collection** | 0 (0%) | 2 (1%) | 0.003 |
| **Conservative management** | | 1 (0.7%) | |
| **US guided tube drainage** | | 1 (0.7%) | |
| **Bile leakage without residual stones** | 1 (2%) | 4 (3%) | 0.065 |
| **Conservative management** | 1 (2%) | 1 (0.7%) | |
| **(ERCP) management** | 0 | 1 (0.7%) | |
| **Surgical management** | 0 | 2 (1%) | |
| **Residual stones management** | 2 (4%) | 9 (7%) | 0.056 |
| **(ERCP)** | 2 (4%) | 7 (5%) | |
| **Surgery** | 0 | 2 (1%) | |
| **Mortality** | 0 (0%) | 0 (0%) | |

**Conclusion:** We encourage the primary **CBD** closure over the use of T-tube as it provides a more comfortable post-operative course, lower morbidity and a shorter hospital stay.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0624 IS LONG-TERM BILIARY STENTING FOR COMMON BILE DUCT STONES SAFER THAN STONE REMOVAL AFTER EST OR EPLBD IN THE ELDERLY?


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**Introduction:** Aged patients with difficulty tolerating prolonged or frequent endoscopic procedure because of poor general condition and prognosis are seen in a rising frequency. Advantages of long-term endoscopic biliary stenting (EBS) with low risk and high safety without stone removal has been pointed out by us in those cases, despite the popular first choice of stone removal in the treatment of common bile duct stones. Endoscopic papillary large balloon dilatation (EPLBD), on the other hand, making it possible to remove a large number of stones in a single procedure, is used in increasing frequency recently.
**Aims & Methods:** In the present study, prolonged EBS on one hand was compared with standard EST and EPLBD with stone removal on the other, to evaluate the safety and indication of these procedures. Test subjects consisted of 740 patients with common bile duct stones older than 80 years in age, subjected to endoscopic treatment in our hospital over the past 12 years (mean age of 87.3 years, maximum age 108 years). EST with stone removal was performed in 370, long term EBS in 349 and EPLBD with stone removal in 21 (maximum stone size and number; EST 10.0 mm and 3.1, EBS 14.9 mm and 4.7, EPLBD 14.8 mm and 3.5). Duration of the procedure, days of post-treatment hospital stay, and freguency of short-term complications and long-term complications including recurrence of cholangitis were recorded.
**Results:** 1) Mean treatment time was 40.2 minutes for EST, and 50.5 minutes for EPLBD compared to 21.2 minutes for EBS (significantly shorter at $p < 0.01$). 2) Mean Post-treatment Hospital Stay was significantly shorter for EBS 5.0 than 8.9

**Abstract No: P0625**

| | Placebo | 5–10 mg OCA | 10 mg OCA |
|---|---|---|---|
| **Europe (n)** | **49** | **45** | **51** |
| Primary Endpoint[a] n (%) | 4 (8%) | 23 (51%)*** | 22 (43%)*** |
| ALP Baseline (U/L) LS Mean (SE) at Change 12 Months[b] | 324.3 (113.0) 2.0 (18.3) | 325.0 (97.5) −109.5 (18.3)*** | 333.0 (112.8) −125.6 (18.1)*** |
| Baseline Bilirubin (umol/L) LS Mean (SE) at Change 12 Months[b] | 12.6 (6.8) 1.7 (0.8) | 11.2 (4.6) −1.1 (0.8)** | 11.9 (6.2) −1.5 (0.8)** |
| **North America (n)** | **21** | **20** | **21** |
| Primary Endpoint[a] n (%) | 1 (5%) | 7 (35%)* | 10 (48%)** |
| ALP Baseline (U/L) LS Mean (SE) at Change 12 Months[b] | 332.7 (119.8) −57.8 (17.4) | 332.7 (159.0) −116.4 (17.2)** | 278.1 (68.4) −141.0 (16.8)*** |
| Baseline Bilirubin (umol/L) LS Mean (SE) at Change 12 Months[b] | 10.6 (8.8) 2.2 (1.1) | 8.1 (7.1) 1.1 (1.0) | 10.0 (7.8) 0.0 (1.1) |

days for EST and 7.2 days for EPLBD ($p < 0.05$, $p < 0.01$). 3) Short-term complications were low; 17.3% for EST, 3.2% for EBS and 0.5% for EPLBD. Serious complications consisted of serious pancreatitis after EST (fatal) and perforation in 1 (laparotomized). 4) Long-term recurrence rate for cholangitis (3 years) was distinctly higher in EBS, 55.5% than in EST, 21.5% ($p < 0.01$). Mean recurrence interval of cholangitis was 2.9 years in EBS, significantly shorter than 5.6 years in EST ($p < 0.01$). 5) Recurrent cholangitis was safely treated in each case without mortality.

**Conclusion:** 1) Long-term EBS caused rather frequent recurrence of cholangitis controlled quickly making prompt repetition possible. This is a safe and non-invasive method providing early ambulation. 2) EPLBD also provides an early ambulation even in cases with large stones but requires a long duration of treatment. 3) Long-term EBS is indicated for aged patients with poor prognosis in the absence of prospect of radical cure, especially those intolerable of a time-consuming endoscopic stone extraction. 4) EPLBD appeared to be especially more desirable than long term EBS for those requiring early ambulation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0625 EFFICACY OF OBETICHOLIC ACID IN THE TREATMENT OF PRIMARY BILIARY CIRRHOSIS BY CONTINENTAL REGIONS

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**Introduction:** Obeticholic Acid (OCA) is a potent and selective farnesoid X receptor (FXR) agonist under investigation for treatment of primary biliary cirrhosis (PBC). POISE was a placebo-controlled, double-blind, randomized Phase 3 study examining the efficacy of OCA in patients located primarily in Europe (EU) and North America (NA). Differing regional lifestyles, standards of care and other variables may affect disease state or response to treatment.

**Aims & Methods:** This analysis assesses the efficacy of OCA within the EU and NA. Inclusion criteria: PBC diagnosis, Alkaline phosphatase (ALP) ≥1.67x upper limit of normal (ULN) and/or total bilirubin >ULN to <2x ULN, stable UDCA dose or unable to tolerate UDCA. 216 patients were enrolled and treated with Placebo (PBO; EU, n = 49; NA, n = 21), 5–10 mg OCA daily (titration from 5–10 mg was based on efficacy and tolerability; EU, n = 45; NA, n = 20), or 10 mg OCA daily (EU, n = 51, NA, n = 21). Primary efficacy was assessed by a composite endpoint of ALP <1.67 x ULN, ≥15% reduction in ALP, and normal total bilirubin. P-values compare active treatments to placebo using either a Cochran Mantel-Haenszel test or ANCOVA.

**Results:** Demographics were well balanced between the two regions. In the EU patients, 51% (5–10 mg OCA, $p < 0.0001$) and 43% (10 mg OCA, $p < 0.0001$) met the primary endpoint vs 8% in PBO. In the NA patients, 35% (5–10 mg OCA, $p = 0.017$) and 48% (10 mg OCA, $p = 0.010$) met the primary endpoint vs 5% in PBO. Mean (SD) baseline ALP (U/L) was similar between groups, EU: 327.6 (107.7); NA: 314.2 (121.6). The least squares (LS) mean change (SE) in ALP (U/L) in EU Patients was 2.0 (18.3) in PBO, −109.5 (18.3) in 5–10 mg OCA ($p < 0.0001$), −125.6 (18.1) in 10 mg OCA ($p < 0.0001$). The LS mean change (SE) in ALP (U/L) in NA Patients was −57.8 (17.4) in PBO, −116.4 (17.2) in 5–10 mg OCA ($p = 0.001$), −141.0 (16.8) in 10 mg OCA ($p < 0.0001$). Mean baseline total bilirubin was within normal range for both groups but higher in the EU patients: 11.9 umol/L compared to 9.6 umol/L in NA patients. The LS mean change (SE) in total bilirubin (umol/L) in EU Patients was 1.7 (0.8) in PBO, −1.1 (0.8) in 5–10 mg OCA ($p = 0.001$), −1.5 (0.8) in 10 mg OCA ($p = 0.0001$). The LS mean change (SE) in total bilirubin (umol/L) in NA patients was 2.2 (1.1) in PBO, 1.1 (1.0) in 5–10 mg OCA ($p = 0.356$), 0.0 (1.1) in 10 mg OCA ($p = 0.072$). Baseline values are Mean (SD). *$p < 0.05$, **$p < 0.01$,***$p < 0.0001$. [a]P-values for comparing treatments are obtained using CMH General association test stratified by randomization strata factor. [b]P-value for comparing active treatments to placebo is obtained using an ANCOVA model with baseline value as a covariate and fixed effects for treatment and randomization strata factor.

**Conclusion:** OCA was effective in both regions with significantly more patients meeting the primary endpoint and having large reductions in ALP compared to PBO. Bilirubin levels were generally reduced or maintained in normal ranges.

**Disclosure of Interest:** P. Andreone: Advisory Committees or Review Panels: Janssen-Cilag, Gilead, MSD/Schering-Plough, Abbvie; Speaking and Teaching: Gilead, BMS
F. Nevens: Consulting: MSD, CAF, Intercept, Gore, BMS, Abbvie, Novar-tis, MSD, Eumedica, Janssen, Promethera Biosciences; Grant/Research Support: Ferring, Roche, Astellas, Novartis, Janssen-Cilag, Abbvie
J. Owens-Grillo: Employment: Intercept Pharmaceuticals, Inc.
R. Pencek: Employment: Intercept Pharmaceuticals, Inc.
T. Marmon: Employment: Intercept Pharmaceuticals, Inc.
L. MacConell: Employment: Intercept Pharmaceuticals, Inc.
All other authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00

**PAEDIATRIC: LIVER, BILIARY AND PANCREAS – POSTER EXHIBITION**

## P0626 DIAGNOSTIC ACCURACY OF SHEAR WAVE ELASTOGRAPHY FOR THE ASSESSMENT OF LIVER STIFFNESS IN CHILDREN WITH FATTY LIVER DISEASE

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**Introduction:** Non-invasive assessment of liver fibrosis by ultrasound elastography techniques has received increasing attention as a means to evaluate disease progression in chronic liver disease patients. In this study, we assessed the value of shear wave elastography with Supersonic Shear Imaging (SSI) for the prediction of fibrosis stage in a cohort of pediatric patients with nonalcoholic steatohepatitis.

**Aims & Methods:** Consecutive patients scheduled for liver biopsy were studied by using SSI ultrasound system, a non-invasive method of assessing tissue stiffness. The correlations between laboratory findings, liver stiffness and the fibrosis score were analyzed using logistic regression and receiver operating characteristic curve analyses were performed to calculate area under the receiver operating characteristics curves for the presence of "any" (F≥1) or significant (F≥2) fibrosis.

**Results:** SSI was performed in 68 consecutive biopsy-proven nonalcoholic steatohepatitis patients (38 males, 31 females, age 12.6 ± 2.48 years). At the univariate linear analysis, SSI showed a high correlation with liver fibrosis (rho = 0.840, $P < 0.001$), ALT (rho = 0.387, $P = 0.001$) and AST (rho = 0.375, $P = 0.002$), degree of portal inflammation (rho = 0.428, $P = 0.002$), lobular inflammation (rho = 0.379, $P = 0.006$) and a moderate correlation for degree of histologic steatosis (rho = 0.279, $P = 0.020$) and histological hepatocyte ballooning (rho = 0.339, $P = 0.015$). However in the multivariate linear analysis (including all the aforementioned variables) the strong correlation with SSI was confirmed only for fibrosis stage ($P < 0.001$) (adjusted r2 = 0.73). Overall, SSI correctly classified 57 of 68 patients (84%). In particular, the ROC curve drawn to differentiate "any" fibrosis (F≥1) from absence of fibrosis (F0) yielded an AUROC of 0.92 (95% CI: 0.86–0.98), with an optimal cut-off of 5.1 kPa (sensitivity 86%; specificity 95%). The AUROC value for differentiating significant fibrosis (F ≥2) from fibrosis degree of less than F2 was 0.97 (95% CI: 0.95–0.99), with an optimal cut-off value of 6.7 kPa (sensitivity 88%; specificity 96%).

**Conclusion:** To date this is the largest case series evaluating the accuracy of SSI in children with fatty liver disease. SSI is an accurate and reproducible non-invasive technique detecting efficiently the presence of significant liver fibrosis and, less accurately, mild liver fibrosis in pediatric patients with non-alcoholic fatty liver disease. Larger clinical prospective studies are warranted to confirm SSI accuracy and establish threshold values for fibrosis grading in comparison or in combination with other non-invasive methodologies.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0627 SILYMARIN FOR THE TREATMENT OF NAFLD/NASH: A MOLECULAR IN VIVO STUDY

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**Introduction:** NAFLD is a liver disease without a specific pharmacological therapy. Diet and life style changes are considered the best treatments, but patient compliance is the main limitation of this approach.
**Aims & Methods:** The aim of this work is to study the nutraceutical properties of Silymarin, added to High Fat High Carbohydrates Diet (HFHCD), in a NASH juvenile mice model, to assess if this compound could exert positive effects without modifications in dietary habits. Females and males C57BL/6 mice were fed with HFHCD immediately after weaning. After 8 weeks of diet when animals presented signs of NASH, Silymarin (33 mg/animal/day) was added to HFHCD and administrated for further 12 weeks. Animals exposed only to HFHCD for the same period (20 weeks) were used as control. Silymarin effects were assessed in terms of bodyweight, BMI, insulin resistance (HOMA-IR), lipidemia (total cholesterol, LDL and triglycerides-TG), hepatomegaly, hypertrophy of visceral adipose tissue and liver histology. The hepatic expression of genes involved in fibrosis, inflammation and steatosis was also assessed. Fibrosis was detected also though Sirius Red and Fast Green staining. Hepatic oxidative status was quantified in terms of MDA and GSH/GSSG analysis.
**Results:** The addition of Silymarin to the HFHCD decreased the liver weight and the visceral adipose tissue ($p < 0.001$); glycaemia was also reduced ($p < 0.05$) but not the HOMA-IR, since insulin level remained unchanged. Plasma LDL-C, TG, ALT, AST were significantly reduced ($p < 0.05$). Liver histology showed a reduction of steatosis and fibrosis. At the molecular level, Silymarin decreased significantly ($p < 0.05$) the expression of $\alpha$-SMA (hepatic stellate cells activation marker) and Collagen 1A1 confirming its effect in improving the fibrogenesis. A reduction of Sirius red staining indicating a decrease of collagen deposition ($p < 0.01$) was observed in males. Silymarin also reduced DGAT2 ($p < 0.05$), and MCP1 ($p < 0.05$) gene expression, markers of steatosis and inflammation, respectively. Of notice, inflammation was observed only in males while oxidative stress in HFHCD females. Silymarin decreased MDA and improved the GSH/GSSG ratio ($p < 0.05$), confirming antioxidant properties.
**Conclusion:** The addition of Silymarin to the HFHCD exerts beneficial effects mainly on lipidemia, liver damage and fibrosis possibly related to its anti-inflammatory and antioxidant activity. These data may be clinically relevant to overcome the low compliance of the patient to change dietary habits.
This work was supported by MIUR (Art.13 D. LGS 297/99-Progetto Nutrizione e Salute) and by FIF in house grant.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0628 DIFFICULTIES OF THE WILSON'S DISEASE DIAGNOSIS IN CHILDHOOD AND ADOLESCENCE

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**Introduction:** Wilson's disease (WD) is an autosomal recessive disorder of the copper metabolism. The clinical manifestations are very variable with hepatic (from asymptomatic to fulminant liver failure of cirrhosis), neurological, psychiatric, ocular or other organ involvement. In some cases the diagnostic is difficult and a high degree of suspicion is needed for diagnostic orientation.
**Aims & Methods:** The aim of our study was to analyse the presence of diagnostic criteria for WD in childhood and adolescence. We have retrospectively analysed the data from the patients with WD diagnosed or followed-up in our unit during 2006–2015. The diagnosis was done using the clinical features, Kayser-Fleischer ring presence, copper metabolism tests and genetic analysis of ATP7B gene, following the up-to-date WD guidelines.
**Results:** WD was diagnosed in 47 patients (26 males, 21 females), with mean age at diagnosis of 12.30 years (range from 5 to 18.16 years). The clinical presentation was with hepatic disease in 37 patients (78.72%, three with associated autoimmunity and one as an acute hepatitis), haemolytic anaemia in 7 patients (14.89%, three of them with fulminant liver failure), neurologic in two patients (2.26%) and by screening as a relative of an index case in one patient (2.12%). Two patients with liver presentation developed also neurological disease in evolution. Serum ceruloplasmin was decreased in all, but two patients (mean level 10.63 mg/dl) and 24 h-urinary copper excretion was increased in all, but 6 patients (mean level 619.11 mcg/24h). In four cases the d-penicillamin challenge was used to prove WD and in two cases (with fulminant liver failure) sample was not collected due to fatal evolution. Kayser-Fleisher ring was present only in 9 patients (19.14%). Molecular analysis of ATP7B gene confirmed the disease in 42 patients (89.36%), in four patients no characteristic mutations were found and in one patient just one of the allele was mutated.
**Conclusion:** The majority of the children and adolescents with WD in our population had hepatic manifestations as clinical presentation. The existent criteria (including genetic analysis) permitted the diagnosis with certitude in most of the patients from our cohort. Genetic analysis could confirm the diagnosis of WD, but sometimes the results are coming too late, mainly in cases with fulminant liver failure with bad prognosis without emergency liver transplantation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0629 NON-INVASIVE TOOLS FOR LIVER DISEASE ASSESSMENT IN OBESE CHILDREN

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**Introduction:** Pediatric obesity plays a central role in the etiology of non-alcoholic fatty liver disease (NAFLD), which has become the most common form of chronic liver disease in children. While biopsy remains the golden standard for staging liver disease, several non-invasive tools have been proposed for evaluating it.
**Aims & Methods:** To evaluate the usefulness of Aspartate-aminotransferase to Platelets Ratio Index (APRI) and a point shear wave elastography technique (point SWE) in assessing liver disease in obese children. We conducted a prospective study in 31 children (mean age $11.4 \pm 3.9$, 22.6% girls, mean BMI $22.62 \pm 7.19\,kg/m^2$) divided into 3 groups: obese children ($n = 14$), children with hepatopathies (cystic fibrosis associated liver disease, chronic autoimmune hepatitis, $n = 4$) and controls (normal weight children without liver disease, $n = 13$). Our analyzed variables included aminotransferase levels and platelet count. We performed liver ultrasonography for the assessment of liver steatosis and elastographic measurements of liver stiffness using point SWE – Virtual Touch Tissue Quantification (VTQ), Acuson S2000 Siemens.
**Results:** Overall 22.5% (7/31) children had NAFLD, while 50% (7/14) of the obese children had NAFLD. None of the controls or children with hepatopathies had NAFLD. APRI scores were higher in obese children with NAFLD ($0.2 \pm 0.07$ vs $0.48 \pm 0.16$, $p = 0.009$). VTQ values were similar both in obese children with NAFLD and without NAFLD ($1.37 \pm 0.61$ vs $1.35 \pm 0.72$, $p = 0.3$). For both APRI and VTQ the highest values were found in children with hepatopathies. When compared to the controls, APRI scores were higher in the obese group ($0.32 \pm 0.18$ vs $0.22 \pm 0.11$, $p = 0.16$). We also found higher VTQ values for the obese, when compared with the controls ($1.36 \pm 0.67\,m/s$ vs $1.11 \pm 0.16\,m/s$, $p = 0.5$).
**Conclusion:** APRI and VTQ are useful for liver disease assessment in obese children. VTQ predicts liver disease in obese children, even when ultrasound steatosis or high transaminase levels are not present.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0630 STRUCTURAL CHANGES IN THE LIVER AND FEATURES OF METABOLIC CHANGES IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE COMBINED WITH BILIARY DYSKINESIA

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**Introduction: Introduction** Nonalcoholic fatty liver disease is one of the most common causes of chronic liver disease in children and adults [1]. Hepatic insulin resistance is associated with the accumulation of fat in the liver, but also plays a crucial role in the development of colloidal properties of bile disorders due to a glut and excess production of bile salts [2]. There are numerous studies that insulin resistance is also a direct factor in gallbladder motility [3]. Functional disorder of the gallbladder with sphincter of Oddi disorder, according to the Rome III criteria relating to the functional disorders of the biliary system. The etiology and pathogenesis of these disorders do not fully clarified, and diagnostic criteria rather contradictory. Functional disorder of the gallbladder can be a primary link of the organic diseases of the biliary tract [4]. Studies on the influence of a violation of the functional state of the gallbladder on structural features in children with liver steatosis almost nonexistent.
**Aims & Methods:** Purpose – to study structural changes in the liver and features of metabolic changes in children with nonalcoholic fatty liver disease combined with biliary dyskinesia. Materials and methods – 34 children aged 5 to 17 years were examined for the presence of risk factors of hepatic steatosis. Abdominal ultrasonography was performed to diagnose the functional state of gallbladder. Gallbladder contractility index was calculated based on the preprandial and postprandial gallbladder volumes. The presence of liver steatosis was determined using transient elastography with the help of FibroScan® 502 touch (Echosens, Paris, France) with controlled attenuation parameter (CAP) measurement. Biochemical lipid spectrum of the blood, biochemical quality of bile were investigated. Determination of taurocholic, taurodeoxycholic, glicoholic and

glikodeoxyholic bile acids in bile was conducted using the thin layer chromatography. Patients were divided into 4 groups: 1st group consisted of 7 patients with existing hepatic steatosis and gallbladder hypokinesia (20.5%); 2nd – 6 patients with liver steatosis and gallbladder normokinesia (17.65%); 3rd – 11 patients without hepatic steatosis but with gallbladder hypokinesia (32.35%); 4th – 10 patients without hepatic steatosis but with gallbladder normokinesia (29.4%).
**Results:** Combination of liver steatosis and gallbladder hypokinesia was associated with liver parenchyma stiffness increasing and CAP reached the maximum values ($268.2 \pm 32.7$ dB / m). Patients with gallbladder hypokinesia were characterized by the development of type IIa dyslipidemia. Combination of liver steatosis and gallbladder hypokinesia demonstrated reduction of cholic acid content with tauroholic acid growth and reducing of glikoholic acids in the liver and gallbladder bile portions. There were also observed increasing in conjugated with glycine bile acids concentration. Accordingly the ratio between oxidized and recovered fractions corresponding bile acids was altered that could contribute to changes of bile colloidal stability.
**Conclusion:** The combination of nonalcoholic fatty liver disease with gallbladder hypokinesia is accompanied by both liver stiffness and CAP increase, type IIa dyslipidemia development and bile composition alteration.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0631 A MULTICENTRE REGISTERED CLINICAL TRIAL ON DIAGNOSTIC PRACTICE IN PEDIATRIC PANCREATITIS (PINEAPPLE – PAIN IN EARLY PHASE OF PEDIATRIC PANCREATITIS)


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**Introduction:** The documented incidence of pediatric pancreatitis (PP) is very low, less than 1/100,000 in almost all European countries, whereas it is around 3.6–13.2/100,000 in the USA and Australia. Moreover, there are large differences between the countries: the incidence decreases from the USA and Western Europe to Eastern Europe.
**Aims & Methods:** Our aim is to understand the current practice of diagnosis of PP and to develop EBM guidelines that helps to evaluate (in a reliable and cost efficient way) the necessity of pancreatic enzyme measurement (PEM) and abdominal ultrasonography when a child has abdominal pain. The PINEAPPLE trial is a registered (ISRCTN35618458), multinational observational clinical trial and the prestudy protocol is already published (http://www.ncbi.nlm.nih.gov/pubmed/26641250). The PINEAPPLE-R reviews retrospectively the children (patients under 18) records appearing at ER units, whereas, the PINEAPPLE-P subtrial is a prospective part of the study where detailed patients data are collected, PEM and abdominal imaging are performed in all cases. Until now 23644 patients records/PINEAPPLE-R and 188 patients/PINEAPPLE-P were enrolled from eight pediatric centres.
**Results:** PINEAPPLE-R: We analysed and compared 11733 American and 11911 Central-European patients data. All together 8.3% (1970/23644) of the patients appearing at ER unit had abdominal pain. The incidence of abdominal pain was 6.2% in America whereas 10.4% in Central-Europe. The rate of the transabdominal ultrasonography was similar in America and in Central-Europe (28.2% vs. 31.2%). However, concerning PEM, 8-times more measurement were performed in the USA than in Central-Europe (21.6% (157/728) vs 2.8% (35/1242)). Not surprisingly the incidence of pancreatitis was 6.9 times higher in USA (4/728) than in Central-Europe (1/1242). PINEAPPLE-P: 3 pancreatitis of 188 patients with abdominal pain were diagnosed.
**Conclusion:** The PINEAPPLE-R study clearly shows that the number of PEM performed at ER units are unacceptably low in children, which could be the reason of low incidences of PP. More patients are crucially needed for PINEAPPLE-P in order to develop EBM guidelines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0632 PRELIMINARY RESULTS FROM APPLE STUDY (ANALYSIS OF PEDIATRIC PANCREATITIS). MULTICENTRIC, INTERNATONAL, PROSPECTIVE, CLINICAL TRIAL


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**Introduction:** Despite of the rising incidence of pediatric pancreatitis (PP) in the last decade, there is still lack of information (studies) concerning the management of childhood onset pancreatitis. Most of the guidelines are based on clinical trials performed on adults.
**Aims & Methods:** The Pediatric Section of the Hungarian Pancreatic Study Group aimed to initiate a prospective international observational clinical trial (APPLE – Analysis of Pediatric Pancreatitis) (i) to understand the genetic factors of all forms of pancreatitis occurred under 18 (APPLE-R), and (ii) to collect a critical mass of clinical data and biomedical research samples from children suffering from AP (APPLE-P). The study has (i) been discussed and agreed in our latest international meeting (http://pancreas.hu/sites/info/files/conferences/ALPD2014-Program.pdf), (ii) received the relevant ethical permission, (iii) been registered at the ISRCTN registry (ISRCTN89664974) which is a primary clinical trial registry recognised by WHO. The study is open for all centres. All clinical research forms are available at our webpage http://pancreas.hu/en/studies.
**Results:** APPLE-R: 35 acute (AP), 8 recurrent acute (RAP) and 14 chronic pancreatitis (CP) cases were enrolled yet. Concerning the etiology, biliary and drug-induced 9–9%, trauma, acohol 2–2%, postERCP and anatomic 5–5%, other 14% were identified however 54% of the cases still remained idiopathic. In 35 cases, genetic analyses of PRSS1, SPINK1, CFTR and CTRC genes have been completed. Genetic alterations in PRSS1 were found in 4 cases (all CP), in SPINK1 in 6 cases (3 RAP and 3 CP), in CFTR in 1 case (CP) and in CTRC in 18 cases (5 AP, 6 RAP and 7 CP), In 5 CP patients mutations in two genes were observed (3 SPINK1-CTRC, 1 PRSS1-SPINK, 1 CFTR-CTRC. APPLE-P: no data available yet.
**Conclusion:** Positive genetic alteration was found in 95% of the idiopathic and 47% of the non-idiopathic groups. Our result suggest that genetic testing should be performed in all children suffering from pancreatitis. The study is still ongoing, more patients are crucially needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## TUESDAY, OCTOBER 18, 2016 09:00–17:00
## PANCREAS II – POSTER EXHIBITION

### P0633 RISK STRATIFICATION DEPENDING ON THE TIMING OF TRANSMURAL ENDOSCOPIC DEBRIDEMENT AFTER SEVERE ACUTE PANCREATITIS: A RETROSPECTIVE GERMAN SINGLE CENTER ANALYSIS


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**Introduction:** The mortality due to severe acute pancreatitis (SAP) is mainly caused by late complications such as infected necrosis. In this context, the classic statement, 'ubi pus, ibi evacua' is still valid. Transmural endoscopic debridement is the treatment of choice for post pancreatic infected necrosis. However, there is still no consensus concerning the optimal timing of the transmural endoscopic interventions.
**Aims & Methods:** We sought to determine the interdependence between the timing of the transmural intervention and the mortality rate, severe adverse

events and therapeutic success. A total of 223 patients with severe acute necrotizing pancreatitis received transmural endoscopic debridement from 1999 to 2015. This cohort was divided in 4 groups according to the timing of the intervention (interval from acute pancreatitis to early intervention ≤4 weeks (EI), 5–8 weeks, 9–12 weeks and >12 weeks).
**Results:** EI was associated with a higher mortality rate than interventions after this period (17% vs. 8%, p = 0.0648) and with a significantly lower success rate (76% vs. 89%, p < 0.05). They were generally justified by signs of septic complications, so this subgroup was characterized by significantly more frequent initial ICU treatment as well as higher inflammatory markers at the time of intervention.

| Time of intervention | n | Success | Mortality | Complications | Sepsis | CRP [mg/dl] | Initial ICU |
|---|---|---|---|---|---|---|---|
| **week 0–4** | 53 | 39 (76%) | 9 (17%) | 24 (45%) | 38 (72%) | 21.7 ± 13.3 | 21 (40%) |
| **week 5–8** | 80 | 69 (87%) | 8 (10%) | 36 (45%) | 39 (49%) | 15.2 ± 10.6 | 24 (30%) |
| **week 9–12** | 36 | 32 (89%) | 3 (8%) | 8 (22%) | 18 (50%) | 13.7 ± 9.5 | 7 (9%) |
| **>week 12** | 52 | 48 (92%) | 2 (4%) | 19 (37%) | 7 (13%) | 9.2 ± 9.2 | 2 (4%) |
| **≤4 wk. vs. >4 wk.** | | p < 0.05 | p = 0.0648 | p = 0.3360 | p < 0.0001 | p < 0.0001 | p < 0.01 |

In the EI group patients with lethal outcome had more frequently cardiovascular (33% vs. 5%, p < 0.05), pulmonary (56% vs. 9%, p < 0.01) and/or renal failure (44% vs. 2%, p < 0.01) at disease onset, defined as systolic blood pressure <90 mmHg, paO2 <60 mmHg or mechanical ventilation and serum creatinine level >2 mg/dl, respectively, as compared to surviving patients in this group. Indication for EI was sepsis (lethal outcome: 100%; survivors: 66%; p < 0.05), mean CRP at the time of intervention was 35.2 ± 12.3 mg/dl (lethal outcome) vs. 18.9 ± 11.6 mg/dl (survivors), p < 0.05. The procedure related complication rates did not differ among both groups (44% vs. 45%).
**Conclusion:** Our data show that delayed as opposed to early endoscopic debridement is associated with more favourable outcomes in patients with SAP complicated by infected peripancreatic necrosis. However, the common consensus that interventions should be delayed as long as possible cannot be inferred from these data. The high mortality rate after EI may be due to the severe condition in general of these patients. Under most critical circumstances early transmural interventions may be a life-saving strategy with more than 80% survival. This "early subgroup" comprising our most demanding and complicated patients deserves more detailed and prospective analysis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0634 ACUTE PANCREATITIS IN THE ELDERLY: A CAUSE FOR INCREASED CONCERN? RETROSPECTIVE EVALUATION OF A TERTIARY REFERRAL CENTER

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**Introduction:** Acute pancreatitis is an aggressive and potentially fatal disease. The elderly population is hypothetically at a higher risk for a fatal outcome. Unexpectedly, recent studies have challenged this assumption, stating that although elderly patients may undergo a severe acute pancreatitis course, they present with no increased mortality. We aimed to confirm these findings in a retrospective cohort of acute pancreatitis patients.
**Aims & Methods:** 254 elderly patients (median 77.5 years, range 65–98 years) and 271 controls (median 46, range 15–64 years) with acute pancreatitis admitted to our center were included in this study. Outcomes included mortality, admission to intensive care unit (ICU), length of hospital stay, development of organ failure or persistent organ failure and need for interventional procedures or nutritional support. Statistical analysis was performed with SPSS v21.0.
**Results:** Elderly patients showed higher median Ranson (1, range 0–8 versus 3 range 1–6, p < 0.001) and BISAP scores (0 range 0–3 versus 2 range 0–5, p < 0.001) and longer length of hospital stay (7.5 range 1–33 versus 8 range 1–44, p < 0.001). Mortality (3.4% versus 9.5%, p = 0.008), ICU admission (29.2% versus 53.0%, p = 0.002), organ failure (21.4% versus 52.6%, p < 0.001), persistent organ failure (8.1% versus 16.9%, p = 0.008) and need for interventional procedures (21.1% versus 66.0%, p < 0.001) were also similar in the older population. There was no difference in the length of ICU stay (p = 0.944) or the need for nutritional support (p = 0.444). In logistic regression analysis, every ten years increase in age increased the risk of death by 10.35 (95%CI 10.12–10.59, p = 0.003).
**Conclusion:** In our series, older age was strongly associated with a more severe course of acute pancreatitis. Early recognition and prompt action are essential in this condition. Especial consideration should be given in older patients as the rates of organ failure and persistent organ failure are higher and the need for interventions is significantly increased.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0635 ENDOSCOPIC AND PHARMACOLOGICAL PROPHYLAXIS OF POST-ERCP PANCREATITIS: A META-ANALYSIS AND SYSTEMATIC REVIEW

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**Introduction:** Post-ERCP pancreatitis (PEP) is the most common complication following endoscopic retrograde cholangiopancreatography. To provide clinical guidance and a framework for future research in this important field, we performed a systematic review and meta-analysis of the global literature on PEP prevention.
**Aims & Methods:** PubMed, Embase, Science Citation Index, Ovid and the Cochrane Controlled Trials Register were searched by 2 independent reviewers to identify full-length, prospective, randomized, control trials (RCTs) published up until March 2016 investigating the use of pancreatic duct (PD) stents and pharmacological agents to prevent-PEP.
**Results:** Twelve RCTs comparing the risk of PEP after PD stent placement (1369 subjects) and thirty RCTs comparing pharmacological agents over placebo (10251 subjects) met the inclusion criteria and were selected for final review and analysis. Meta-analysis showed that prophylactic pancreatic stents decreased the odds of post-ERCP pancreatitis (OR, 0.28; 95% CI, 0.18–0.42). Pooled analysis showed a significant OR reduction of PEP with rectal administration of Diclofenac (OR, 0.24; 95% CI, 0.12–0.48) compared with placebo. Rectal administration of Indometacin compared with placebo significantly decreased the odds of PEP (OR, 0.59; 95% CI, 0.44–0.79), with significant heterogeneity observed (P = 0.045; $I^2$ = 56%). Subgroup analysis showed a significant reduction with bolus administered somatostatin (OR, 0.23; 95% CI, 0.11–0.49).
**Conclusion:** Pancreatic stent placement, rectal Diclofenac and bolus administration of somatostatin are most effective in preventing post-ERCP pancreatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0636 THE UTILITY OF SIRS AND BISAP SCORES FOR PREDICTING SEVERITY, MORBIDITY AND MORTALITY IN PATIENTS WITH ACUTE PANCREATITIS

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**Introduction:** A high Systemic Inflammatory Response Syndrome (SIRS) score at admission and a persistently high SIRS at 48 hours have been shown to predict a severe course, presence of pancreatic necrosis, ICU stay and mortality in acute pancreatitis. The Bedside Index for Severity of Acute Pancreatitis (BISAP) Score has been used as predictor of mortality in acute pancreatitis (AP). SIRS can be easily calculated in the emergency room and is also a component of the BISAP score.
**Aim**: The aim of this study was to compare the performance of BISAP with SIRS alone in predicting severity, mortality, length of hospital stay, ICU stay, organ failure, infections and need for interventions in patients with acute pancreatitis.
**Methods**: Consecutive patients admitted with acute pancreatitis from June 2013 to July 2015 were included in the study. A retrospective analysis of prospectively collected data from all patients was carried out. SIRS and BISAP were calculated at admission to the emergency room. As per the Revised Atlanta Classification the patients were classified into Mild, Moderately Severe and Severe Acute Pancreatitis.

**Abstract No: P0636**
**Table 1:** Clinical Characteristics of the two groups

| | SIRS ≤ 1 (n = 37) | SIRS ≥ 2 (n = 38) | P value | BISAP ≤ 1 (n = 40) | BISAP ≥ 2(n = 35) | P value |
|---|---|---|---|---|---|---|
| **Mild Moderately severe Severe** | 31 4 2 | 12 17 9 | 0.0001 | 36 4 0 | 7 17 11 | 0.0002 |
| **Age (years)** | 40.78 ± 17.6 | 39.6 ± 18.1 | 0.69 | 35.3 ± 15.6 | 45.1 ± 19.4 | 0.01 |
| **M/F** | 31/6 | 30/8 | NS | 33/7 | 28/7 | NS |
| **Duration of hospital stay (days)** | 4.86 ± 4 | 11.2 ± 9.7 | 0.0004 | 4.8 ± 3 | 11.9 ± 10.2 | 0.0001 |
| **ICU stay (days)** | 1 ± 1.97 | 4.5 ± 5.9 | 0.001 | 0.75 ± 1.2 | 5 ± 6.1 | 0.0001 |
| **Organ failureTransientPersistent** | 0 2 | 5 9 | 0.0014 | 0 0 | 5 11 | 0.0001 |
| **InfectionPancreaticExtrapancreaticBoth** | 1 0 1 | 2 3 4 | 0.04 | 0 0 0 | 3 3 5 | 0.0001 |
| **Mortality** | 0 | 3 | 0.24 | 0 | 3 | 0.09 |
| **Need for intervention** | 4 | 5 | 1 | 2 | 7 | 0.07 |

**Results:** Seventy-five patients with AP (mean age 40.3 years) were included in the study, 81.3% were male. Forty-three patients (57.3%) had mild AP, 21 patients (28%) had moderately severe AP and 11 patients (14.7%) had severe AP. Three patients with acute severe pancreatitis died, no mortality was seen in the mild AP or moderately severe AP groups. Sixteen patients (21.3%) developed organ failure, 5 patients had transient organ failure and 11 patients had persistent organ failure. Eleven patients (14.67%) developed infections. Six patients developed either pancreatic or extra-pancreatic infection alone, whereas 5 patients developed infection at both pancreatic and extra-pancreatic sites. SIRS $\geq$ 2 at admission had a sensitivity of 81.2 (95%CI 63.5 to 92.8%), specificity of 72% (95% CI 56.3 to 84.6%), PPV 68.4%(95% CI 51.3 to 82.5%) and a NPV of 83.8% (95% CI 67.99 to 93.8%) to predict a moderately severe/severe course of AP. In comparison, BISAP $\geq$ 2 at admission had a better PPV of 80% (95% CI 63 to 91.5%) and NPV of 90% (95% CI 76.3 to 97.2%). The sensitivity and specificity of BISAP $\geq$ 2 was 87.5% (95% CI 71 to 96.4%) and 83.7% (95% CI 69.3 to 93.2%) respectively. BISAP $\geq$ 2 was more accurate in predicting a severe course of AP when compared to SIRS $\geq$ 2 (85.3% vs 76%). Patients with BISAP $\geq$ 2 or SIRS $\geq$ 2 had a significantly longer hospital and ICU stay, higher rate of infection and organ failure (Table 1). Mortality and need for interventions was similar in both the groups.
**Conclusion:** The SIRS and BISAP scores are easy to calculate and both scores can be used for risk stratification of all patients with acute pancreatitis. SIRS $\geq$ 2 and BISAP $\geq$ 2 at admission both correctly predict a severe course of AP, however the BISAP score is more accurate. Both scores accurately predict a longer hospital and ICU stay, greater risk of organ failure and infections in patients with acute pancreatitis. Patients with SIRS $\geq$2 or BISAP $\geq$2 at admission need close monitoring and should be considered for referral to a pancreatic unit.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0637 A NEW SCORING SYSTEM TO PREDICT POST-ERCP PANCREATITIS

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**Introduction:** Post-ERCP pancreatitis (PEP) can be sometimes serious and/or fatal. Therefore, it is important to detect high risk patients for adequate preventive strategies. Some risk factors for PEP are known, but there are few reliable methods for predicting whether PEP will develop in an individual patient [1].
**Aims & Methods:** The aim of this study is to develop a practical prediction rule for PEP. This study was designed as hospital-based observational study. From April 2010 to September 2012 at Kyoto University Hospital, Kitano Hospital and Yodogawa Christian Hospital, patients who were referred for transpapillary ERCP were enrolled. Exclusion criteria were under 18 years old, patients with clinical evidence of acute pancreatitis at the time of the procedure, and patients with altered gastrointestinal anatomy. e.g. Roux-en-Y reconstruction. The main outcome was PEP. In addition, we assessed two types of candidate predictive factors. (1) Patient-related factors included younger age ($<$60 years), female gender, history of PEP, chronic pancreatitis, jaundice, periampullary diverticulum, intact papilla and suspect of sphincter of Oddi dysfunction. (2) Procedure-related factors included difficult cannulation (over 15 min), endoscopic sphincterotomy, precut sphincterotomy, endoscopic papillary balloon dilation and pancreatic contrast injection, biliary drainage, pancreatic drainage, stone extraction, common bile duct intraductal ultrasonography (C-IDUS), pancreatic duct IDUS, tissue sampling (biopsy and brushing cytology) from biliary tract and tissue sampling from pancreatic duct. Univariable analysis and multivariable logistic regression were used to detect candidate predictive factors for PEP. Based on the analysis, we constructed several scoring models by changing the detailed settings of model construction. The final model was selected from those candidate models based on the area under the receiver-operating characteristic curve (AUC), visual inspection of the histogram and clinical adequacy.
**Results:** Result from 2738 patients were analyzed. PEP developed in 133 cases (4.9%), 80 mild, 46 moderate, 6 severe and 1 fatal. By univariable analysis, 8 candidate factors were selected; younger age, female gender, history of PEP, intact papilla, difficult cannulation, pancreatic contrast injection, C-IDUS, and tissue sampling from bile duct. Multivariable risk factors with adjusted odds ratios (OR) were female gender (OR: 1.5 [95% CI, 1.1–2.2]), history of PEP (OR: 4.1 [95% CI, 2.0–8.0]), intact papilla (OR: 2.9 [95% CI, 1.8–4.9]), difficult cannulation (OR: 2.32[95% CI, 1.6–3.5]), pancreatic contrast injection (OR: 2.6 [95% CI, 1.7–4.1]),and C-IDUS/tissue sampling from biliary tract (OR:2.1 [95% CI, 1.4–3.1]). A scoring system was constructed from the six clinical variables as below. Female gender: 1 point, history of PEP: 3 points, intact papilla: 2 points, difficult cannulation: 2 points, pancreatic injection: 2 points, C-IDUS/tissue sampling from biliary tract: 1 point. The points were added up to a total score that predicts the risk of pancreatitis. Cases scoring 2 or fewer points had less than a 2% risk of PEP. Those scoring 3 and 4 points had 3.9–5.9% risk, while those scoring 5 between 7 points had 10.3–17.5% risk and more than 7 points had more than 20% risk. AUC of this model was 0.80. When all cases were divided into two groups; a low risk group (scoring 4 points or fewer) and a high risk group (more than 4 points). The sensitivity of this criteria was 66.9%, specificity was 78.3%, positive predictive value was 14% and negative predictive value was 97.8%. All patients with severe PEP belonged to a high risk group.
**Conclusion:** The present study found that female gender, history of PEP, intact papilla, difficult cannulation, pancreatic contrast injection, and C-IDUS/tissue sampling from biliary tract independently increased the risk of PEP. This scoring system will serve as a useful prognostic tool for PEP in clinical practice, although it requires prospective validation with a variety of patients and clinicians.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0638 EFFICACY OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN FOR DISTURBANCES OF COAGULATION AND PANCREATIC ISCHEMIA/NECROSIS IN SEVERE ACUTE PANCREATITIS

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**Introduction:** Severe acute pancreatitis (SAP) is a potentially high-mortality disease for which organ. Organ failure (OF) is among the chief causes of mortality. Pancreatitis-related OFs are either local or systemic. In general, local OF can be divided into three stages: pancreatic ischemia, pancreatic necrosis, and walled-off necrosis (WON). Pancreatic necrosis is caused by pancreatic ischemia, which leads to WON. Systemic OF, including shock states, respiratory failure, renal failure, and heart failure, is the common origin of patient instability. Both local and systemic OFs can be caused by disturbances of coagulation and inflammatory effects. These SAP disorders are related to the development of disseminated intravascular coagulation (DIC). Recombinant human soluble thrombomodulin (rTM) was recently approved for use in treating sepsis- induced DIC[1]. According to a recent study, SAP patients with disturbances of coagulation and treated with rTM showed significantly lower rates of development of WON than those not treated with rTM[2].
**Aims & Methods:** This study investigates whether rTM improves the disturbances of coagulation in SAP, and prevents the development of pancreatic ischemia/necrosis. We retrospectively analyzed 87 successive patients with SAP treated at our hospital from January 2006 to December 2015 at Osaka Saiseikai Nakatsu Hospital. All patient data was gathered from an electronic database. A diagnosis of SAP was determined using the Japanese severity scoring system. The study enrolled patients with SAP whose treatment began within 48 hours of onset. Eighty-seven SAP patients were divided into two groups: SAP patients treated with rTM (380U/kg for 30 min, once daily) (rTM group, 42 patients) and not treated with rTM (control group, 45 patients). JAAM DIC scores, as the coagulation abnormality, were calculated before treatment (admission day = day 0) and after the start of treatment (days 3 and 7). A diagnosis of pancreatic ischemia/necrosis based on conventional contrast-enhanced CT (CECT) was recorded. We assessed the development of WON 4 weeks later based on CT/MRI.
**Results:** On day 0, the condition of patients in the rTM group was significantly worse than the control group in age ($69.8 \pm 14.2$ vs. $61.2 \pm 17.8$ years), APACHE II score ($11.6 \pm 3.8$ vs. $9.1 \pm 5.1$), SOFA score ($4.0 \pm 2.8$ vs. $2.7 \pm 2.5$), and number of OF patients {42.9 (18/42) vs. 17.8 (8/45) [%]} ($p < 0.05$). On day 0, we found no significant differences in rate of pancreatic ischemia/necrosis between the rTM group and the control group {64.3% (27/42) vs. 60.0% (27/45), $p = 0.82$}. On day 0, we found significant differences in coagulation abnormality between the rTM group and the control group (rTM vs. control: $4.8 \pm 1.6$ vs. $2.6 \pm 1.6$ for JAAM DIC score; $51.2 \pm 38.1$ vs. $20.2 \pm 17.6\,\mu g/mL$ for FDP; $27.1 \pm 21.1$ vs. $14.7 \pm 14.2\,\mu g/L$ for TAT; $13.5 \pm 10.0$ vs. $5.6 \pm 4.9\,\mu g/mL$ for D-dimer; $p < 0.05$). On day 7, the following parameters fell for patients treated with rTM: JAAM DIC scores, FDP levels, TAT levels, and D-dimer levels. Univariate analysis shows that identified platelet counts, FDP levels, D-dimer levels, JAAM DIC score did not significantly contribute to pancreatic ischemia/necrosis. A multivariate analysis was performed, incorporating the factors identified by univariate analysis. The JAAM DIC score ($P = 0.047$, OR = 0.651, 95%CI: 0.427–0.995) was the only factor found to contribute to the absence of pancreatic ischemia/necrosis.
**Conclusion:** In this study, lower JAAM DIC scores were related to the absence of pancreatic ischemia/necrosis, a local complication. Treatment with rTM immediately improved disturbances of coagulation, including JAAM DIC scores. rTM may be a candidate as a new therapeutic option beneficial in addressing local complications for SAP patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0639 NEW FULLY COVERED LARGE-BORE REMOVABLE METAL STENT – WITH ANTI-MIGRATORY FLANGES FOR DRAINAGE OF PANCREATIC FLUID COLLECTIONS: RESULTS OF A SINGLE CENTER EXPERIENCE

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**Introduction:** Endoscopic transmural drainage (ETMD) of peripancreatic fluid collections(PFC) is an effective alternative to surgical drainage. Conventional drainage using plastic stents has its limitations. Removable wide bore, short metal stents have been used successfully in the past for this purpose, but spontaneous stent migration and tissue erosion secondary to the stents have been reported.
**Aims & Methods:** Assesment of efficacy and safety of a newly designed fully covered bi-flanged metal stent (BFMS) with special anti-migratory flanges and with internal diameter of 14 mm (Hanaro, MI Tech, South Korea) for ETMD. This was a retrospective analysis of prospectively collected data in a single center with adequate experience in EUS guided ETMD. Parameters evaluated were technical success of stent placement, clinical success as defined by radiological resolution of PFC and resolution of symptoms. Feasibility of endoscopic necrosectomy and stent removal was noted. Adverse events including stent migration and stent related tissue erosion were recorded. Patients were followed up with suitable imaging to confirm PFC resolution. Stents were endoscopically removed within six weeks of placement after confirmation of clinical and radiological resolution of PFC.
**Results:** Twelve patients of PFC underwent endoscopic ultrasonography (EUS) guided ETMD using this BFMS underduring a five month period (July – October 2015). Ten were males. Mean age was 37 years (20 – 65). Alcohol was commonest etiology of pancreatitis (8/12, 67%). Nine PFCs were pseudocysts (PPC's) and three were walled off necrosis (WON) with significant debris in the cavity. Technical and clinical success for drainage was seen in all patients (100%). Direct endoscopic necrosectomy (DEN) was performed in 3 (25%) patients. No adverse events were observed. There were no incidences of stent migration or stent related tissue erosion. Mean duration of follow up was10 weeks (4 – 20). All stents were removed within six weeks of placement. At the time of writing the abstract, 4/12(33%) patients had undergone stent removal.
**Conclusion:** The new specially designed anti- migratory BFMS is safe and effective for drainage of PFC. Endoscopic necrosectomy can be carried out through the stent. Stent can be removed endoscopically at the end of the treatment period. No incidences of spontaneous stent migration or stent related tissue erosion were noted in this small series of patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0640 METABOLIC SYNDROME AND ACUTE PANCREATITIS

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**Introduction:** The aim of our study was to investigate the influence of metabolic syndrome on the course of acute pancreatitis determined by disease severity, the presence of local and systemic complications and survival rate.
**Aims & Methods:** 609 patients admitted to our hospital in the period from January 1, 2008 up to June 31, 2015 with the diagnosis of acute pancreatitis were analyzed. The diagnosis and the severity of acute pancreatitis were made according to the revised Atlanta classification criteria from 2012.
**Results:** Of 609 patients with acute pancreatitis, 110 fulfilled the criteria for metabolic syndrome. Patients with metabolic syndrome had statistically significantly higher incidence of moderately severe (38.2% vs. 28.5%; $p = 0.05$) and severe (22.7% vs. 12.8%; $p = 0.01$) acute pancreatitis in comparison to those without metabolic syndrome, while patients without metabolic syndrome had higher incidence of mild acute pancreatitis in comparison to those patients with metabolic syndrome (58.7% vs. 39.1%; $p < 0.001$). Patients with metabolic syndrome had a higher number of local and systemic complications, and higher APACHE II score in comparison to patients without metabolic syndrome. In multivariable logistic regression analysis, the presence of metabolic syndrome was independently associated with moderately severe and severe acute pancreatitis. Comparing survival rates, patients suffering from metabolic syndrome had a higher death rate compared to patients without metabolic syndrome (16% vs. 4.5%; $p < 0.001$).
**Conclusion:** The presence of metabolic syndrome at admission portends a higher risk of moderately severe and severe acute pancreatitis, as well as higher mortality and longer duration of stay in intensive care unit. Given the rising incidence of metabolic syndrome, we can expect even higher incidence of severe acute pancreatitis in the near future. Regarding the fact that most of metabolic syndrome components can be either prevented or improved through lifestyle changes and/or pharmacological agents, a question is raised whether this can also prevent the occurrence of acute pancreatitis, namely severe acute pancreatitis and its complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0641 INVOLVEMENT OF GENETIC FACTORS IN THE AETIOLOGY OF ALCOHOLIC CHRONIC PANCREATITIS

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**Introduction:** In Western countries, alcohol abuse is the main aetiology of chronic pancreatitis (CP), representing 70% to 80% of cases. However, only less than 10% of heavy drinkers develop CP. The discovery of involvement of certain genes such as PRSS1, CFTR and SPINK1 in hereditary and idiopathic CP, also raises the question of the role of genetic factors in alcoholic chronic pancreatitis (ACP). Several studies have been conducted in recent years to search this involvement, especially regarding PRSS1, SPINK1, CLDN2 and more recently, CEL, ABO and FUT-2.
**Aims & Methods:** The aim of this work is to investigate whether genetic factors may be protective against the development towards CP or conversely may promote the evolution to CP in alcoholic subjects. A case-control study was conducted. The group of cases included 40 severe alcoholics with CP whilst the group of controls included 76 severe alcoholics without CP. Severe alcoholics were defined to have an alcohol consumption of more than 80 g per day for at least 5 years. DNA extraction was performed from a blood sample taken from each participant. Genotyping of PRSS1, SPINK1, CLDN2, ABO and FUT-2 variants of interest was achieved by a High Resolution Melting (HRM) method. The recently described CEL-HYB allele was genotyped using the previously published long-range duplex PCR assay followed by sequencing.
**Results:** The Single Nucleotide Polymorphism (SNP) rs10273639 of PRSS1 is more frequently found among alcoholics controls ($OR = 0.12$, $CI_{95\%} = [0.04–0.42]$; $p < 0.0001$). The SNP rs12688220 of CLDN2 is significantly associated with ACP ($OR = 2.83$; $CI_{95\%} = [1.08–7.49]$; $p = 0.02$). The SPINK1 p. N34S variant was identified in only 3 cases in the heterozygous state, or 7.5% of cases. The CEL-HYB allele was found in the heterozygous state in 2 cases out of 40 examined (5%). Of the 76 alcoholic controls studied, one carried this hybrid allele in the heterozygous state, or 1.32%. As for SNP rs8176693 of ABO and SNP rs632111 of FUT2, no observable differences of allele frequency were found between cases and controls.
**Conclusion:** This study has allowed us to demonstrate a protective effect of the rs10273639 in PRSS1 and a predisposing effect of rs12688220 of CLDN2. The suggestive predisposing effect of SPINK1 p. N34S variant (as well as the CEL-HYB allele) remains to be tested in larger samples. However, we did not detect any distribution differences of the ABO and FUT2 variants between cases and controls. Recruitment of alcoholic subjects is going in order to confirm or otherwise our results. The identification of susceptibility and protective genes in ACP will allow not only better knowledge of disease initiation and progression but also improved therapeutic management.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0642 IS SURGERY USEFUL TO CURE CHRONIC PAIN IN ALCOHOLIC CHRONIC PANCREATITIS?

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**Introduction:** Chronic pain is a severe symptom in chronic pancreatitis (CP), leading to morphine addiction and reduced quality of life. Pancreatic surgery is usually performed as a last resort therapeutic option and its outcomes are still widely debated.
**Aim**: To assess pancreatic surgery results performed for chronic pain in patients with alcoholic CP and to determine pathological and morphological markers of therapeutic response.
**Methods**: All patients with alcoholic CP who underwent pancreatic surgery for chronic pain between 2008 and 2015 were included. Clinical data such as tobacco, alcohol and analgesics intake, type of surgical procedure, quality of life (QOL) data at 6 months and 1 year, radiological and pathological features were analyzed.
**Results:** 50 patients were included (men, 88%; age at surgery, 47 years old (32–64)). Surgical procedures were resections (Frey procedure, distal pancreatectomy or whipple procedure; $n = 45$) or drainage (lateral pancreaticojejunostomy $n = 5$). All patients were smokers (pack-year, 30 (10–90)). Postoperative tobacco and alcohol withdrawals were observed in 40% and 80% of the patients, respectively. Opioid intake before surgery, at 6 months and at 1 year was 60 mg (20–500), 20 mg (0–360) and 0 mg (0–360), respectively. QOL at 6 months and 1 year was respectively good (52% vs 54%, NS), average (34 vs 24%, $p = 0.01$) and bad (14 vs 22%, $p = 0.01$). The median delay between CP diagnosis and surgery was 5

years (1–22). Early surgery was associated with lower postoperative opioid intake ($r = 0.35$, $p = 0.01$) opioid withdrawal at 6 months (5.87 versus 4.5 years $p = 0.03$) and at 1 year ($p = 0.09$). At 6 months, opioid withdrawal was associated with an absence of exocrine ($p = 0.06$) and endocrine ($p = 0.08$) pancreatic insufficiency, a pre-operative alcohol withdrawal ($p = 0.08$), an improved quality of life and postoperative smoking cessation ($p = 0.0075$) but not with the type of surgery, nor morphological inflammation. Pathological (neuritis, lymphocytes infiltration, nerve hyperplasia) and radiological (inflammation, pseudocyst, calcifications) features were not associated with postoperative pain changes. Optimal delay between CP diagnostic and surgery allowing opioid withdrawal at 6 months and 1 year was 2 years. Following multivariate analysis, predictive factors for opioid withdrawal at 6 months were a surgery performed within 2 years (OR = 4.228 (1.04–17.17)) and a postoperative smoking cessation (OR = 3.561 (1.021–12.41)). At 1 year, only smoking cessation was predictive for opioid withdrawal, OR = 11.33 (2.677–47.98).
**Conclusion:** A benefit (opioid withdrawal and improved quality of life) depends mainly on complete postoperative smoking cessation and early surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0643 BELGIAN NATIONWIDE REGISTRY ON CHRONIC PANCREATITIS: A PROSPECTIVE OBSERVATIONAL STUDY OF MORE THAN 800 PATIENTS

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**Introduction:** Epidemiology of chronic pancreatitis (CP), as well as natural history, complications and therapeutic management are variable and not well described on a national basis.
**Aims & Methods:** This multicenter prospective observational study including 8 Belgian hospitals could improve the knowledge of these aspects. All patients with CP proven by imaging procedures were eligible. 809 patients were included between 1/9/2014 and 31/8/2015 using a case report form completed once at the time of out-patient visit or in-patient admission. Data collected included epidemiological, etiological items as well as CP complications (exocrine and endocrine insufficiency, pain) and type of treatment.
**Results:** Among the 809 patients, 794 were aged 16-year-old (adult population); the 15 remaining patients consisted the pediatric population. Characteristics of the adult population were the following: a majority of male (74%) and outpatient inclusion rate (69%), mean age at symptoms onset was 46 years and duration of disease was 9 years, median Izbicki pain score (IPS) was 96 (0–195). Main etiological risk factors according to TIGARO classification were alcohol and tobacco (69%) followed by idiopathic cause in 17%. Recurrent acute pancreatitis, genetic, auto immune and obstructive causes were less represented, between 2–4%. Pancreas divisum was identified in 3% of the cases. More patients had stopped alcohol than smoking (47 vs 21%). Benefits from no alcohol abuse were: higher BMI (25 vs 22 $kg/m^2$, $p < 0.01$), lower Izbicki pain score (90 vs 121, $p < 0.01$) and lower inability to work. Benefits from tobacco withdrawal were higher BMI (25 vs 22 $kg/m^2$, $p < 0.01$) and lower Izbicki pain score (82 vs 137, $p < 0.01$). Endocrine and exocrine insufficiencies were reported in 41% and 36% respectively. Diabetes was significantly more important in toxic cause than the others (44 vs 35%, $p < 0.05$) while there was no significant difference concerning exocrine insufficiency. Patients with BMI < 20 $kg/m^2$ had significantly more exocrine insufficiency (44 vs 34%), weight loss (32 vs 16%), pain (IPS: 146 vs 75) and included more current smokers (78 vs 46%) and alcohol drinkers (30 vs 15%), ($p < 0.001$). Concerning the impact of treatment on pain, patients with ongoing endoscopy were associated with highest Izbicki pain score (163/400) compared to patients with previous or no endoscopic treatment (83, 82/400 respectively) as well as patients with initial surgical management without endoscopy (79/400), ($p < 0.001$). 14% of patients had previous surgery and among them, 25% had initial surgery without previous endoscopic treatment. There was a majority of duodenopancreatectomy (30%) or partial resection (19%) followed by pancreatico-jejunostomy (13%). In children, there was a majority of girls (73%); idiopathic and genetic causes were the main risks factor (54 and 34% respectively). A majority of them were under the percentile 50 in the BMI for age percentiles curve. No diabetes and exocrine insufficiency were reported.
**Conclusion:** This nationwide Belgian study about 809 CP patients could provide a useful tool to emphasize the management of these patients in terms of complications and treatment. Cessation of smoking and alcohol and BMI > 20 $kg/m^2$ were associated with better outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0644 MANAGEMENT OF PANCREATOLITHIASIS: A NATIONWIDE SURVEY IN JAPAN

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**Introduction:** Prevalence of patients with chronic pancreatitis has been increasing in Japan. Chronic pancreatitis often is associated with pancreatolithiasis. When pancreatic stones develop, pancreatic ductal hypertension can cause pain and pseudocysts, thereby further exacerbating the disease condition. Treatment of pancreatic stones is extremely important. Although surgical and endoscopic treatments remain the conventional therapies for pancreatolithiasis, usefulness of extracorporeal shock-wave lithotripsy (ESWL) has been recognized. In 2014, an application for health insurance coverage of ESWL was approved by the government. We performed a 2-part nationwide survey of prevailing practices in management of pancreatolithiasis.
**Aims & Methods:** In the first part, replies from 566 of 1683 institutions with more than 200 beds were obtained, among these, 282 hospitals treated 4653 patients with pancreatolithiasis between 2009 and 2013. In the second part, clinical data were collected from 1835 patients treated for pancreatolithiasis at 125 hospitals. Patients included 1477 men and 358 women (gender ratio, 4.1). Mean age was 59.9 years (range, 9 to 99). Most often, chronic pancreatitis was alcohol-related (65.4%), idiopathic was the next most common category (17.6%). Statistical analyses included chi-squared tests. Differences associated with probability (p) values below .05 were considered significant.
**Results:** ESWL alone was performed in 103 patients (5.6%); ESWL plus an adjunctive endoscopic procedure (endoscopic sphincterotomy, endoscopic pancreatic sphincterotomy, or endoscopic balloon dilation) 446 (24.3%); endoscopic treatment alone 261 (14.2%); and surgery 168 (24.3%). Other therapies including pancreatic enzyme replacement, antispasmodic drugs, or protease inhibitors, were given to 358 (19.5%). No treatment was considered in 499 (27.2%). Fragmentation of all stones was achieved in 447 of the 549 patients undergoing ESWL (81.4%). Stone clearance was complete in 49.9% of patients treated by ESWL with or without adjunctive endoscopic treatment, and in 48.3% of patients treated only endoscopically. Symptom relief rate was 85.7% after ESWL including adjunctive endoscopic treatment, 80.8% after endoscopic treatment alone, and 92.9% after surgery. Early complication rates within 3 months after ESWL including adjunctive endoscopic treatment, endoscopic treatment alone, and surgery were 8%, 4.5%, and 26.9%, respectively. Rates of late complications occurring over 3 months after ESWL including adjunctive endoscopic treatment, endoscopic procedures alone and surgery were 1.7%, 2.5%, and 8.2%, respectively. Symptom relief rate but also, early and late complication rates for surgery were significantly higher than for ESWL and endoscopic treatment. Among 417 patients treated with ESWL, 61 (14.6%) required surgery, as did 32 (16%) of 200 patients treated endoscopically. Reoperation was required in 11 (6.7%) of 165 patients who were treated with surgery. Need for operation was significantly less frequent after surgery than that for surgery after the other treatments.
**Conclusion:** In Japan, non-surgical treatments were chosen more frequently than surgical treatment for patients with pancreatolithiasis. Appropriate guidelines for clinical management of pancreatolithiasis should improve efficacy and safety
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0645 EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY FOR PANCREATIC DUCT STONES IS EFFECTIVE IN TERMS OF PAIN RELIEF AND USE OF OPIOIDS

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**Introduction:** Fragmentation of pancreatic duct stones (PDS) using extracorporeal shock wave lithotripsy (ESWL) allows flow of pancreatic juice, spontaneous passage of small stone fragments, and facilitates endoscopic removal of

larger stones. Studies have shown that ESWL is effective in terms of lowering pain intensity and improving the quality of life. However, studies on use of analgesics before and after the ESWL are limited.
**Aims & Methods:** All consecutive ESWL procedures performed in our department in the period August 2010 to December 2014 were reviewed. We extracted data on demographics, technical details, pain score, and use of analgesics before and after ESWL. Data on the use of analgesics was obtained from hospital records, electronic medicine database, and prescription database. Our aim was to evaluate the use of analgesics before and after the ESWL.
**Results:** Ninety-six patients received 157 (1–7 per patient) ESWL procedures. The mean age was 57 years, 64% being males. Alcohol was the cause of chronic pancreatitis in 71% of the cases. There was a significant reduction in the daily use of opioids, before and after ESWL, and a significant increase in patients with no pain and no use of analgesics, see Table 1. The number and location of stones did not affect the use of analgesics. Table 1 shows the use of analgesics before and after the ESWL.

| Pain and analgesic use | Before ESWL | After ESWL | P-value |
|---|---|---|---|
| No pain and no use of analgesics | 11% | 39% | $<0.0001$ |
| Mild pain but no use of analgesics | 5% | 3% | 0.49 |
| "As needed" use of weak analgesics | 7% | 9% | 0.75 |
| Daily use of weak analgesics | 5% | 3% | 0.49 |
| "As needed" use of opioids | 18% | 17% | 0.90 |
| Daily use of opioids | 54% | 29% | 0.0006 |

**Conclusion:** ESWL is an effective and opioid-saving procedure in the management of pain in patients with PDS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0646 MALNUTRITION IS A COMMON COMPLICATION IN CHRONIC PANCREATITIS OUTPATIENTS AND SIGNIFICANTLY ASSOCIATED WITH IMPAIRED MUSCLE FUNCTION

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**Introduction:** Malnutrition is a well-known complication of chronic pancreatitis (CP), but little is known about its prevalence, risk factors and health-related consequences in the outpatient setting.
**Aims & Methods:** We investigated the prevalence of malnutrition in CP outpatients and its associated risk factors and influence on muscle function and quality of life. This was a cross-sectional study of CP outpatients. We used bioelectric impedance to measure body composition, and a handheld dynamometer (hand grip strength) and the timed up and go test to investigate muscle function. The EORCT QLQ C30 questionnaire was used to document quality of life. The primary outcome was malnutrition defined as a body mass index $<18.5\,kg/m^2$.
**Results:** A total of 166 patients with CP were enrolled in the study. The median age was 58.6 years (IQR 49.9–66.1) and 70% were men. The prevalence of malnutrition was 10.8% (95% CI; 6.6–16.6). Opioid use ($P=0.036$), exocrine pancreatic insufficiency ($P=0.025$) and female sex ($P=0.041$) were identified as independent risk factors. Patients with malnutrition had decreased handgrip strength compared to patients with normal nutritional state ($28.7\pm11.3$ kPa vs. $38.5\pm12.3$ kPa; $P=0.0016$) and used a longer period of time to complete the time up and go test ($10.3\pm4.6$ sec vs. $8.2\pm4.0$ sec; $P=0.026$). Lean body mass and handgrip strength was significantly correlated ($r=0.57$; $P<0.001$) and this correlation was further strengthened when analysing the patients with malnutrition independently ($r=0.83$; $P<0.001$). Global health status was comparable between groups ($P=0.76$).
**Conclusion:** Malnutrition is a common complication in CP outpatients and significantly associated with impaired muscle function.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0647 "DUODENAL DYSTROPHY", OR "GROOVE PANCREATITIS", OR "PARADUODENAL PANCREATITIS." DOES IT MATTER WHICH NAME YOU CHOOSE? LESSONS OF 71 CASES

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**Introduction:** Different terms were proposed as an umbrella for cystic dystrophy in heterotopic pancreas (duodenal dystrophy, DD), paraduodenal cyst and groove pancreatitis, by reasoning that these conditions mimic pancreatic head tumors and share certain histological evidences. The reasons for amalgamation of these terms in "paradudenal pancreatitis (PD)" are unclear.
**Aims & Methods:** To understand the origin of the DD assessing results of different treatment modalities by 1.prospective analysis of 71 cases of PP or DD (2004–2015), comparing 71 preoperative and 54 histopathological findings; 2. Assessment of clinical presentation and the results of DD treatment.
**Results:** Preoperative diagnosis was correct in all the cases except one, when cystic tumor of the pancreatic head was suspected (1.9%). Patients were presented with abdominal pain (100%), weight loss (76%), vomiting (30%) and jaundice (18%). CT, MRI and endoUS were the most useful diagnostic modalities. Ten patients were treated conservatively, 31 underwent pancreaticoduodenectomies (PD), pancreatico- and cystoenterostomies (8), Nakao procedures (4), duodenum-preserving pancreatic head (DPPH) resections (5), and 12 pancreas-preserving duodenal resections (PPDR). No mortality. Full pain control was achieved after PPRDs in 91%, PDs in 83%, and after DPPHR resections and draining procedures in 18% of cases. Diabetes mellitus developed thrice after PD. In 3 PD cases only moderate pancreatitis was revealed in specimen.
**Conclusion:** 1. Early diagnosis of DD saves pancreas; 2. Late diagnosis "convert" DD in PP and leaves patient only PD; 3. The effectiveness of PPDR proves that DD is an entity of duodenal, but not paraduodenal origin.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0648 GLYPICAN-1 IDENTIFIES CANCER EXOSOMES AND DETECTS VARIOUS DIGESTIVE SYSTEM NEOPLASMS

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**Introduction:** Exosomes are kinds of nanovesicles secreted by both healthy and unhealthy cells. They are about 30–100 nm wide and can be found in most of the body fluids, including blood, urine, saliva, breast milk, and so on[1]. The exosomes have been found to contain various proteins and nucleic acids, and play a central role in cancer development[2]. In addition, the proteins and nucleic acids contained in exosomes are less easy to be degraded and had more quantitative advantages as biomarkers comparing the circulating RNAs or DNAs. The heparin sulfate proteoglycan glypican-1 (GPC1) is a membrane anchored protein and has found to be universally and highly expressed in breast cancer[3], pancreatic cancer[4], human gliomas[5], ameloblastoma[6], neuroendocrine tumors[7], and some other solid tumors. Melo et al. and his colleagues found that GPC1 was enriched on pancreatic cancer-cell-derived exosomes[8]. GPC1+ circulating exosomes (crExos) were detected in the serum of pancreatic cancer patients with absolute sensitivity and specificity. It was also found that the level of GPC1+ crExos was correlated with tumor burden and prognosis, indicating GPC1+ crExos may serve as a potential biomarker for pancreatic cancer diagnosis[8].
**Aims & Methods:** In this study, we isolated crExos from patients with pancreatic carcinoma ($n=64$), esophageal squamous cell carcinoma (ESCC, $n=61$), gastric cancer ($n=54$), colorectal cancer ($n=42$), healthy donors ($n=30$), gastrointestinal polyp patients ($n=30$), and pancreatitis patients ($n=7$), and performed flow cytometry (FACS) analysis of crExos of these patients to detect GPC1 protein expression level.
**Results:** We found that digestive tumor exosomes are enriched in GPC1. The GPC1+ crExos level may be a reliable biomarker for detecting of digestive cancer, especially pancreatic carcinoma and CRC. The diagnostic value of GPC1+ crExos is superior to the traditional tumor marker, such as CA199, CEA, and AFP.
**Conclusion:** In summary, we found that GPC1+ crExos level may be a reliable biomarker for detecting of digestive cancer, and the diagnostic value of GPC1+ crExos is superior to the traditional tumor marker, such as CA199, CEA, and AFP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.
duodenal dystrophy, groove pancreatitis, paraduodenal pancreatitis, chronic pancreatitis

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## P0649 PANCREATIC CANCER DIAGNOSTIC BIOMARKERS-FROM LITERATURE TO CLINICAL TESTING

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**Introduction:** Establishing the diagnosis of pancreatic ductal adenocarcinoma (PDAC) is important for optimal patient management but can be difficult and relies on imaging and cytology/pathology. A tissue diagnosis is not obtained in a significant proportion of PDAC cases. Hence, an unmet clinical need exists for the diagnosis of PDAC from cytology samples. One potential way of improving the diagnosis is to use immunohistochemistry (IHC) biomarkers as an adjunct to cytology in difficult to diagnose cases.
**Aims & Methods:** A systematic approach was used to identify and validate the best available biomarkers. In the identification phase, a meta-analysis of potential IHC biomarkers investigated in PDAC was performed with sensitivity and specificity as outcome variables. High ranking candidates from meta-analysis were validated by IHC on tissue microarrays (TMAs) of surgical specimens from 99 patients with PDAC. Sensitivity and specificity analyses were performed based on five potential cut-offs from the data generated from TMAs. Two cut-offs namely, 10% positive cells and 20% positive cells were investigated for observer agreement amongst seven pathologists. Finally, high ranking candidates using 10% cut-offs were investigated in twenty cytology samples and sensitivity and specificity analyses were performed.
**Results:** Sixteen biomarkers identified in systematic review were quantified in meta-analysis and the highest ranked biomarkers were KOC, maspin, S100P, mesothelin and MUC1. These biomarkers showed the following sensitivity & specificity in surgical specimens using 10% cut-off: KOC 87% & 97%; S100P 86% & 97%; mesothelin 94% & 88%; MUC1 90% & 35%; and Maspin 98% & 98%. Analysis of a panel of KOC, S100P and mesothelin achieved almost 100% sensitivity and specificity if at least two biomarkers were positive for both 10% and 20% cut-offs.
The investigation of 10% and 20% cut-offs for observer agreement showed reasonable strength of agreement (Kappa $>0.50$) modestly decreasing inter and intra-observer variability in IHC interpretation but 10% is slightly better than 20%. Finally, in cytology samples, 10% cut-off achieved higher sensitivity & specificity values: KOC 92% & 100%; maspin 54% & 100% and mesothelin 72% & 100%. In addition, analysis of a panel of KOC, maspin and mesothelin achieved 82% sensitivity and 100% specificity for 10% cut-off in cytology samples.
**Conclusion:** A panel of KOC, maspin and mesothelin is a suitable diagnostic panel and 10% cut-off is a reasonable cut-off achieving high observer agreement. Their diagnostic accuracies approach those of optimal conventional cytology. These markers may be appropriate for further clinical validation and potentially routine use in difficult cases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0650 REAL-LIFE USE OF INTENSIFIED CHEMOTHERAPY FOR METASTATIC PANCREATIC CANCER IN EUROPE

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**Introduction:** Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer-related death in Europe. Gemcitabine has been the standard of care for patients with metastatic PDAC. Recently, FOLFIRINOX and nab-paclitaxel+gemcitabine have shown significant survival benefits compared to gemcitabine in clinical trials.
**Aims & Methods:** This study aims to investigate the efficacy of FOLFIRINOX and nab-Paclitaxel+gemcitabine versus gemcitabine monotherapy or gemcitabine-based doublets (gemcitabine+erlotinib, +5-FU, +capecitabine or +cisplatin) in real-life clinical care across different European institutions and to analyze the decision making process among physicians administering these drugs. We conducted a retrospective multinational study including patients with metastatic PDAC receiving palliative chemotherapy from January 2012 through January 2015. In addition, we utilized a web-based questionnaire study, containing 15 questions regarding use of chemotherapy in metastatic PDAC, was sent to 5420 doctors in 19 European countries in June 2015.
**Results:** 634 patients from 8 centers in the UK, Germany, Italy and Hungary were included of which 55% (351) were male and 15% (97) underwent primary resection before systemic recurrence. Analysis showed that Gem-based regimens without nab-Paclitaxel were frequently used in European centers from 2012–2015 (75% vs. 9% for FOLFIRINOX and 3% for nab-Paclitaxel+gemcitabine; 13% other regimens). The median overall survival (OS) in different groups were: FOLFIRINOX 12.0 months (95% CI 8.5–15.5), nab-Paclitaxel + gemcitabine 7.0 months (95% CI 4.7–9.3), other gemcitabine doublets 9.0 months (95% CI 7.4–10.6) and gemcitabine monotherapy, 5.0 months (95% CI 4.4–5.6). FOLFIRINOX was associated with improved survival ($p < 0.001$). 153 valid responses from the questionnaire from 19 countries were analyzed. As first-line therapy, 47% used nab-Paclitaxel+gemcitabine, 42% used FOLFIRINOX and 11% used gemcitabine+/-erlotinib in 2015. Of the intensified regimens, dose reductions were more common for FOLFIRINOX likely due to higher toxicity, as FOLFIRINOX was estimated to be more toxic than nab-Paclitaxel+gemcitabine (neutropenia 88% vs. 68%; polyneuropathy 42% vs. 41%; rapid deterioration 42% vs. 31%). FOLFIRINOX was rated over nab-Paclitaxel+gemcitabine in achieving longer survival with acceptable quality of life (52% vs. 44%, respectively).
**Conclusion:** Intensified regimens are widely available throughout Europe, but used variably in clinical routine dependent on hospital setting and country. A large multicenter retrospective series of patients revealed that in spite of the improvement and availability of intensified regimens, gemcitabine-based treatments were predominantly used in 2012–2015. However, the pan-European questionnaire revealed a more frequent use of intensified regimens indicating an increasing acceptance among European doctors in 2015. In line with previous clinical trial data, nab-Paclitaxel+gemcitabine appears to have a more favorable toxicity profile compared to FOLFIRINOX, and needed de-escalation less often.
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## P0651 ENDOSCOPIC ULTRASOUND-GUIDED HYBRIDTHERM ABLATION IN PATIENTS WITH STAGE III PANCREATIC DUCTAL ADENOCARCINOMA: PROSPECTIVE SINGLE CENTER COHORT STUDY

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**Introduction:** 30–40% of patients (pts) with pancreatic adenocarcinoma (PDAC) are not resectable at the diagnosis because of locally advanced disease. Standard treatment is Chemotherapy (CT) ± Radiotherapy (RT). We evaluated feasibility and safety of endosonography-guided HybridTherm ablation (EUS-HTP) in a preliminary report, showing a trend in tumor size reduction[1].

**Aims & Methods:** Primary aim was to assess the effect of EUS-HTP on tumor growth. Secondary aims were to evaluate tumor induced necrosis and to determine overall survival after EUS-HTP. Consecutive pts with stage III PDAC after CT ± RT were prospectively enrolled and treated by EUS-HTP at our tertiary referral Center. The HTP, a flexible bipolar device combining radiofrequency with cryogenic cooling, was used under EUS guidance. The tumor growth, evaluated by the absolute volume of the tumor mass (ATV), the necrotic volume of the ablated area (ANV), and the overall survival (OS) were evaluated by a radiological and clinical follow-up. Data were analyzed using descriptive statistics and non-parametric tests for group differences and correlation analysis. P-values $< 0.05$ were considered as statistically significant.

**Results:** 35 pts with stage III PDAC were enrolled (21 M; mean age 63.66 years). EUS-HTP was feasible in 26 pts (74.3%); it was not possible in 9 pts because of tumor stiffness or vessel interposition. Six pts received two or more treatments. The application time was dependent on the tumor size ($R = 0.45$; $p = 0.038$) with a mean duration of 125.90 sec (range 30–360). Early complications occurred in 11/26 pts (42%), all mild, except one moderate (endoscopic intervention). Late complications were reported in 6/26 pts (23%), of which 5 were mostly related to tumor progression. CT scans were able to measure the lesion volumes in 25/26 treated pts (96%). No significant changes in the ATV were observed at post-treatment evaluation (mean 44.5 days: $31.65 \pm 26.2$ mm$^3$), compared to the pre-treatment CT scan evaluation ($29.9 \pm 24.5$ mm$^3$). The mean ANV was 12.44 mm$^3$ (range 1.3–56), i.e. 34.9% (range 3–65) of the tissue could be ablated by HTP. There was a significant positive correlation between ablation time and ANV ($R = 0.66$, $p = 0.013$) and also a significant positive correlation between ANV and ATV ($R = 0.92$, $p < 0.0001$). The longer the ablation duration and the larger the ATV were, the larger was the ANV. An analysis of the median survival time for pts treated only once and for those treated two or more times revealed an increase of the survival time from 5 to 9 months ($p = 0.066$). The median post-EUS-HTP OS was 6 months (range 1–22), with 2 pts still alive (3 and 9 months after EUS-HTP).

**Conclusion:** EUS- HTP is a safe treatment, able to obtain disease stability and may improve the mean survival time. These positive results suggest the possibility to include EUS-HTP in the treatment algorythm of stage III PDAC after CT ± RT.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0652 WORLDWIDE SURVEY ON OPINIONS AND USE OF MINIMALLY INVASIVE PANCREATIC RESECTION

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**Introduction:** The introduction of minimally invasive pancreatic resection (MIPR) into surgical practice has been slow. Randomized trials in this field are lacking. While valuable and informative, existing cohort studies suffer from selection biases and surgeon opinion. Worldwide utilization of and attitudes towards MIPR remains unknown.

**Aims & Methods:** We developed an international survey in order to gain knowledge on opinions and use of MIPR. The anonymous survey was send out online using Google Docs (Google, Mountain View, CA) to all surgeon members of the International Hepato-Pancreato-Biliary Association, Asian-Pacific Hepato-Pancreato-Biliary Association, Americas Hepato-Pancreato-Biliary Association, European-African Hepato-Pancreato-Biliary Association, Japanese Society of Hepato-Biliary-Pancreatic Surgery and PancreasClub. The survey consisted of 61 questions focusing on both laparoscopic and robot-assisted pancreatic resection; and included demographic information, experience with MIPR, patient selection criteria, learning curve estimates, presumed effect of MIPR on health-care costs, patient quality of life, and education in MIPR. Non-responders received up to two reminders.

**Results:** In total, 435 surgeons from 50 countries completed the survey. Median surgical experience was 12 (Interquartile range (IQR): 6–20) years and responders performed a median of 22 (IQR: 0–450) pancreatic resections as primary surgeon annually. Minimally invasive distal pancreatectomy (MIDP) was performed by 345 (79%) surgeons with a total personal experience of median 20 (IQR: 10–50) MIDPs. Of surgeons performing MIDP, 338 (98%) surgeons considered the overall value of MIDP superior or equivalent to the open approach. Minimally invasive pancreatoduodenectomy (MIPD) was performed by 124 (29%) surgeons with a total personal experience of median 12 (IQR: 4–40) MIPDs. Of surgeons performing MIPD 96 (77%) surgeons considered the overall value of MIPD superior or equivalent compared to the open approach. The most important reason for not performing MIPR was a lack of specific training. 161 (37%) surgeons received training in MIPR whereas 275 (63%) and 350 (81%) felt like they would benefit from training in MIDP or MIPD, respectively. Proctoring on-site was considered as the most important training element by 140 (32%) surgeons and 392 (90%) would consider participation in an international registry.

**Conclusion:** This worldwide survey on MIPR showed that the median annual number of MIPRs performed per surgeon is low. Whereas most surgeons considered MIDP superior or equivalent to open distal pancreatectomy, this was less clear for MIPD. Specific training in MIPR, especially on-site proctoring, with outcomes monitored by an international registry seems required.

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## P0653 WATCHFUL FOLLOW-UP IS ACCEPTABLE, BASED ON CLINICAL OUTCOMES OF MAIN DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

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**Introduction:** In the IPMN/MCN international consensus guidelines 2012, main duct IPMN (MD-IPMN) with main pancreatic duct (MPD) dilation of 5–9 mm considered as one of the "worrisome feature" have changed from rather immediate resection to more deliberate observation and evaluation. In the previous guideline, surgical resection is strongly recommended for all surgically fit patients, so natural course for MD-IPMN has been limited and still unclear.

**Aims & Methods:** The aim of this study was to clarify the natural history of MD-IPMN without surgical resection. Method; 1012 patients with IPMNs were treated in our institute from April, 1996 to December, 2014. 43 patients were with MD-IPMN. 32 patients without surgical resection and more than 1 year imaging follow-up were identified and their cases reviewed retrospectively. Evaluation points were 1) initial clinical data, 2) progression rate, 3) outcomes.

**Results:** Of 32 patients, mean age was 75.3 years and male was 56%. Median observation period was 48.2 months (17.2–153.8 months). 1) The initial median size of the MPD dilation is 10 mm (4–25), 14 patients with "worrisome feature", 18 patients with "high-risk stigmata", 4 patients had mural nodules. 2) 14 patients (43.8%) of 32 exhibited progression. 6/14 among "worrisome feature" group, 8/18 among "high-risk stigmata" group. The details of progression were 13 cases with an increasing MPD diameter, 2 cases with an increasing cyst size, and 6 cases with appearance and/or enlargement of mural nodules (included overlapping). Median period to progression was 26.6 months (4.9–98.9). 3) Surgical resection was performed in 4 of 14 patients with progression.3 patients were died (1 of invasive IPMC, 1 of pancreatic cancer and 1 of cancer of other organ). Progression rate by the Kaplan Mayer Curve was 25.5% for 2 years and 48.0% for 5 years.
**Conclusion:** This study suggested we could expect clinical course and progression rate for MD-IPMN without surgical resection and it is no significant difference of progression rate between "Worrisome feature" group and "High-risk stigmata" group. Both group could have been observed, if malignant findings (mural nodule > 5 mm etc.) were not revealed. It is highly important that we decide how long we observe patients with MD-IPMN and when we suggest surgical resection to them.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0654 SYSTEMATIC REVIEW OF RESECTION RATES AND CLINICAL OUTCOMES AFTER FOLFIRINOX-BASED TREATMENT IN PATIENTS WITH LOCALLY ADVANCED PANCREATIC CANCER

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**Introduction:** FOLFIRINOX prolongs survival in patients with metastatic pancreatic cancer and may alsobenefit patients with LAPC of which a substantial number may convert into resectable tumors. Previous studies combined LAPC and borderline resectable pancreatic cancer, which hampers the interpretation of outcomes with FOLFIRINOX in LAPC.
**Aims & Methods:** The aim of this review is to provide an overview of the (R0) resection rate and clinical outcomes after FOLFIRINOX-based therapy for locally advanced pancreatic cancer (LAPC). PubMed, Embase and Cochrane were systematically searched for studies published up to August31st, 2015. Primary outcome was (R0) resection rate.
**Results:** Fourteen studies involving 365 patients with LAPC were included. A modified chemotherapy regimen was described in 3 studies and FOLFIRINOX dose reductions in up to 65% of patients. Radiotherapy was given in 57% of all patients. Total resection rate was 28% (77% R0). Mediano verall survival ranged from 8.9 to 25.0 months. Median survival after resection was 24.9 months. Six out of 85 (7%) resection specimens showed a complete pathologic response. Grade 3–4 toxicity occurred in 23% of patients. The resection rate of patients treated with FOLFIRINOX without radiotherapy was 12% (70% R0) with 15.7 months median overall survival and 19% grade 3–4 toxicity.
**Conclusion:** FOLFIRINOX-based treatment for patients with LAPC seems safe and achieves high (R0) resection rates and overall survival, despite the frequent administered modified regimes and dose reductions during treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0655 CLINICAL EFFICACY OF PET/CT IN PATIENTS WITH INCREASED SERUM CA19–9 WITHOUT BILIARY TRACT OR PANCREATIC MALIGNANCY

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**Introduction:** Serum CA19–9 level is considered a useful tumor marker for biliary tract and pancreatic malignancy. But, CA 19–9 can be elevated in benign lesion also.
**Aims & Methods:** This study was to determine the clinical efficacy of $^{18}$F-FDG (fludeoxyglucose F 18)-PET/CT in patients with increased serum CA19–9 level without biliary tract or pancreatic malignancy. We enrolled 78 patients who received PET/CT after serum CA19–9 elevation (> 37 U/ml) without biliary tract or pancreatic malignancy. We divided patients into two groups based on whether FDG uptake on PET/CT could explain the cause of CA19–9 elevation.
**Results:** In 45 of 78 patients, the CA19–9 elevation was explained by FDG uptake on PET/CT. Most malignancies were detected by PET/CT except one case. Acute CA19–9 elevation over 200 U/ml for duration of 6 months was an independent factor for diagnostic PET/CT finding. Ten of 45 patients had CA19–9 elevation explained by PET/CT which other screening tests produced inconclusive results. These patients were female and nine cases involved benign diseases.
**Conclusion:** To patient with increased serum CA19–9 level without biliary tract or pancreatic malignancy, PET/CT could be a useful method for explaining the cause of CA19–9 elevation even when other screening tests produced inconclusive results. And CA19–9 elevation over 200 U/ ml for duration of 6 months had greater diagnostic value on PET/CT regardless of malignant or benign disease status.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0656 A PROSPECTIVE COMPARATIVE STUDY OF THE 'SUCTION METHOD' VERSUS THE 'NO SUCTION PLUS SUCTION METHOD' IN ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION OF MALIGNANT PANCREATIC SOLID MASSES

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**Introduction:** In recent years, EUS-FNA as been noted for its high diagnostic accuracy and is on the road to becoming established as a clinically useful technique. On the other hand, there is a need to establish a more safe and efficient method for specimen collection in order to prevent the development of procedural accidents and collect high-quality specimens for genetic exploration. In the present study, we focused on the suction method for collecting specimens by EUS-FNA. The author proposes a method combining the suction and no-suction methods, and compared it with the conventional method in terms of collection of adequate specimens from malignant solid pancreatic tumors.
**Aims & Methods:** The study was conducted in 65 patients who underwent EUS-FNA after providing written consent for this study and received a final diagnosis of malignant solid pancreatic tumor between May 2013 and January 2016. Either 22- or 25-G needles for puncturing, and 20-mL suction syringes were used. Both the "no-suction plus suction method" (NS+S method), consisting of 5 strokes without suction and 10 strokes with suction, and the conventional suction method (S method), consisting of a total of 15 strokes with continuous suction, were used in all the patients. A pathologist conducted microscopic examinations of the specimens under the blinded condition. The adequate specimen collection rate, diagnostic accuracy rate and the level of blood contamination of the tissue specimens were prospectively compared between the two methods.
**Results:** In all, 74 cytology specimens were collected by the NS+S method and 78 cytology specimens by the S method, and a total of 67 histology specimens was collected by the NS+S method and 72 specimens by the S method. The adequate specimen collection rate for cytologic diagnosis was 94.6% by the NS+S method and 98.7% by the S method ($p = 0.15$), and that for histologic diagnosis was 74.6% by the NS+S method and 81.9% by the S method ($p = 0.29$), with no statistically significant difference between the two methods. The overall diagnostic accuracy rate in this study based on the combination of cytology and histology was 89.2% (58 of 65 patients). In a comparison between the NS + S and S methods, the diagnostic accuracy rate based on the combination of cytology and histology was 72.3% for the NS+S method and 86.1% for the S method ($p = 0.052$), tending to be higher for the S method. The low level of blood contamination in the tissue specimens was 40.3% for the NS+S method and 23.6% for the S method ($p = 0.03$), being significantly lower in the NS + S method, especially tumor size ≥29 mm and with a 22 G needle.
**Conclusion:** The NS + S method may allow higher-quality specimens with less blood contamination compared to the S method. However, the optimal suction/no-suction ratio and optimal number of strokes should be determined.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0657 ENDOSCOPIC ULTRASONOGRAPHY OF THE PANCREAS REFLECTS EXOCRINE AND ENDOCRINE FUNCTION

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**Introduction:** Non-alcoholic fatty liver disease or non-alcoholic steatohepatitis occurs after pancreatic resection as a result of decreased pancreatic function. Predicting postoperative pancreatic dysfunction and measuring postoperative nutritional complications are important for quality of life. However, pancreatic function tests such as the pancreatic function diagnostic (PFD) test and 75 g oral glucose tolerance test (OGTT) require great care and are not performed in all patients. Endoscopic ultrasonography (EUS) is a popular and less invasive diagnostic tool that shows detailed pancreatic structures. Structural changes correlate with function, therefore, detailed EUS findings are expected to reflect pancreatic function. However, to the best of our knowledge, there are no reports about correlations among pancreatic parenchymal changes shown by EUS, exocrine function and endocrine function. We analysed the correlation between EUS images and the results of the PFD test and 75 g OGTT.
**Aims & Methods:** We analysed 46 patients who underwent pancreatic resection for pancreatobiliary disease. There were 28 men and 18 women, with a mean age of 60 years. Primary diseases were as follows: invasive ductal carcinoma

(n = 16), chronic pancreatitis (n = 12), intraductal papillary mucinous neoplasm (n = 10), bile duct carcinoma (n = 6), serous cystadenoma (n = 1) and mucinous cystadenoma (n = 1). Surgical procedures included pylorus-preserving pancreaticoduodenectomy (n = 31), distal pancreatectomy (n = 8), segmental resection (n = 6), and duodenum-preserving pancreatic head resection (n = 1). All cases were examined during the inactive pancreatitis phase by EUS, and exocrine function was measured by PFD and endocrine function by 75 g OGTT. EUS findings were divided into three types: Group I, high-echoic dots with a small and similar size; Group II, large and homogeneous macule pattern; and Group III, nodular pattern with inhomogeneous sizes.
**Results:** Six patients had Group I EUS findings, 17 had Group II findings, and 23 had Group III findings. The mean results of the PFD test for each group were as follows: Group I, 91%; Group II, 73%; and Group III, 55%, with a significant difference between each group. Correlation between EUS patterns and glucose intolerance by 75 g OGTT was: Group 1, 17%; Group II, 29%; and Group III, 67%. There were significant differences between Groups I and III, and Groups II and III.
**Conclusion:** EUS patterns reflected pancreatic exocrine and endocrine function. EUS images are expected to predict remnant pancreatic function.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0658 ENDOSCOPIC ULTRASOUND (EUS) HAS THE EDGE OVER CT/MRI IN THE DETECTION OF PANCREATIC NEURO-ENDOCRINE TUMOURS (PNETS) IN PATIENTS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE I (MEN1)

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**Introduction:** Early identification of pNETs is a key element to reducing morbidity and mortality in MEN1 patients. Prognosis is associated with tumour size. Many pNETs are small subcentimetre lesions and only become symptomatic when the tumour is large. Conventional radiology is suboptimal in detecting such lesions, thus missing the window to remove them at an earlier stage.
**Aims & Methods:** We compared: (a) linear-EUS detection of pNETs in patients with confirmed MEN1 vs triple-phase contrast-enhanced CT/MRI pancreas and (b) incremental benefit of EUS to cross-sectional imaging for detection of small pNETs and quantity of pNETs in this cohort. Between Jan 2008- Oct 2015, a total of 20 patients with clinically confirmed MEN1 underwent baseline assessment with EUS, CT/MRI and biochemical screening. Data were retrospectively retrieved from the hospital electronic records database. Statistical analysis was performed using SPSS v20 on the size and number of pNET detection by EUS and CT/MRI using the Wilcoxon Signed Rank Test and McNemar Chi-square.
**Results:**

Detection of pNETs in MEN-1 cases

| | CT/MRI pancreas | EUS |
|---|---|---|
| Median pNET size (mm) | 14.5 | 7.1 |
| Smallest pNET size (mm) | 12.7 | 4.6 |
| Total pNETs Detected (%) | 57.9% | 100% |

A total of 28 EUS procedures and an equal number of cross-sectional imaging (CT/MRI) were performed. pNETs were identified in 95% of all 20 MEN1 cases. Overall median pNET size was 7.1 mm on EUS and 14.5 mm on CT/MRI ($p = 0.007$). Median value for smallest pNETs detected by EUS was 4.6 mm and 12.7 mm on CT/MRI ($p = 0.001$). EUS detected more pancreatic lesions/pNETs compared to CT/MRI ($p < 0.001$) in 25 of the 28 procedures (89.3% more). The remaining 3 procedures showed equal numbers of pNETs detection by both modalities. The interquartile range (IQR) for smallest pNET detected by EUS was 3.0–5.0 mm while IQR for CT/MRI lies between 8.3 mm-14.8 mm. EUS detected all 100% cases of pNETs in our series of MEN1 compared to CT/MRI imaging alone which detected 57.9% cases ($p = 0.008$). 14 of 20 patients had FNA performed with a positive yield of 85.7%. In 50% of patients, pNET measured $\leq$10 mm.
**Conclusion:** In MEN1 patients, CT/MRI underestimated the presence of pNETs in approximately half of all cases compared to EUS and was not able to identify small pNETs ($<$ 8 mm) in all but one case. EUS offers higher sensitivity than cross-sectional imaging (CT/MRI) in terms of detecting the number of positive pNET cases as well as a greater number of pancreatic lesions especially subcentimetre ones. EUS should be considered a standard tool in the algorithm for MEN1 workup, instead of an adjunct reserved for diagnostic dilemmas.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0659 THE RELATIONSHIP BETWEEN GASTROENTEROPANCREATIC NEUROENDOCRINE NEOPLASM (GEP-NEN) PROGNOSIS RE-STRATIFICATION AND KI-67 VARIABILITY: A SINGLE CENTER STUDY

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**Introduction:** Ki-67 is increasingly recognized as a prognostic factor for gastroenteropancreatic neuroendocrine neoplasm (GEP-NEN). The cutoff index of Ki-67, especially for G3 type, is the current hot topic on grading of GEP-NEN. The characteristics of Ki-67 variability and the correlation to the prognosis of GEP-NEN have not been well evaluated.
**Aims & Methods:** A total of 225 GEP-NEN patients treated in Wuhan University Hospital between 2009–2015 were enrolled and reviewed. All the specimens, clinic information, follow-up and survival dada were collected. The correlation among Ki-67 index, the variability of Ki-67 and prognosis of disease were evaluated. The decision tree methods, Kaplan-Meier methods and Cox regression analysis were used.
**Results:** The re-grading of NEN using the Ki-67 index (intervals 0–27.5% ; 27.5–55% ; 55–75% ; 75–100%) in our cohort suggested a risk stratification and prognosis in high-proliferation type of G2-NEN and G3-NEN graded by the WHO classification. Comparing the primary with metastasis specimens, Ki-67 index were elevated in 45% cases and were down-regulated in 10% patient. Ki-67 index keep stable in 45% NEN patients. The rectum was the most variable primary site. While, the G3-NEN present the most variable intervals. The group with Ki-67 variability had a worse prognosis relative to the group without Ki-67 variability ($P = 0.0074$). The GEP-patient could be separated with a promising three-dimensional model as Ki index, variability of Ki-67 and tumor location.
**Conclusion:** G3-NEN group could be further re-stratification into 3 groups with elevated Ki-67 index and worse prognosis. Ki-67 variability indicates a worse prognosis. Ki index, variability of Ki-67 and tumor location could be three important prognostic factors for NEN. The re-assessment of Ki-67 status in metastatic sites may be important for assessing prognosis of GEP-NEN patients, especially for those with primary G3 tumors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0660 SLIT2-ROBO1 SIGNALLING ACTIVATES RAS TO SUPPRESS METASTASIS, AND IS ASSOCIATED WITH TIME-TO-PROGRESSION IN PANCREATIC NEUROENDOCRINE TUMOURS

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**Introduction:** Slit2 and its receptor Robo1 constitute evolutionary conserved axon guidance cues with repellent function in directing neurogenesis, angiogenesis and endocrine development. Transcriptom analysis revealed that mRNA signatures of distinct metastatic phenotypes in patients with pancreatic NETs (pNETs) exhibit differences in several components of the Slit-Robo signalling pathway.
**Aims & Methods:** We thus aimed at delineating the role of Slit-Robo signalling for tumour biology and progression in pNETs. To this end, expression of Slit2 and Robo1 on human pNET tissues was determined by immunohistochemistry and quantitative PCR. In vitro migration and colony formation, as well as metastasis in an orthotopic pNET mouse model were evaluated using pNET cell lines genetically manipulated for restored Slit2 expression or functional inactivation of Robo1 activity.
**Results:** Quantitative PCR indicated a reduction of Slit2 expression in pNET tissues as compared to healthy pancreas. Immunohistochemistry localized expression of the Slit2 receptor Robo1 to epithelial tumour cells of pNETs and hence identified the tumour epithelial compartment with the capacity to respond to secreted Slit2 ligand. Furthermore, reduction of Robo1 mRNA tissue levels correlated to shorter time-to-progression in pNET patients. To experimentally address the function of Slit2-Robo1 signalling, BON and QGP pNET cell lines with divergent endogenous expression of Slit2 were used. Restored Slit2 expression in Slit2-deficient BON cells inhibited proliferation, transwell migration and colony formation in softagar assays. Conversely, disruption of Slit2-Robo1 signalling via lentiviral Robo1 knockdown or sequestration of endogenous Slit2 in QGP cells by a soluble Robo1 decoy receptor stimulated directed migration and colony formation of QGP cells. Mechanistically, restored Slit2-Robo1 signalling in BON cells stimulated, whereas functional inactivation of Robo1 in QGP cells reduced Ras activity. As a consequence of Ras activation, expression of yes-associated protein (YAP) was enhanced, and cell cycle progression was delayed in BON cells with restored Slit2 expression, consistent with a growth suppressive function of Ras in endocrine cells. Conversely, Ras activity rather promoted neuroendocrine differentiation as evidenced by an increase of chromogranin A release by BON cells upon re-expression of Slit2. Ultimately, the incidence of lymphatic metastases and lymphangiogenesis were reduced in mouse orthotopic BON tumours with restored Slit2 expression.
**Conclusion:** Our experimental and translational data assign to Slit2-Robo1 a novel function as metastasis suppressor and identified Ras and YAP as downstream mediators, which link Slit2-Robo1 signalling to growth inhibition and neuroendocrine differentiation. Together, we provide functional evidence, that loss of Slit2-Robo1 activity in pNETs may contribute to a metastatic phenotype in pNET patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0661 NATURAL HISTORY AFTER LONG-TERM FOLLOW UP OF PANCREATIC NEUROENDOCRINE TUMORS (PNET), BASED ON THE DETECTION OF THE PROLIFERATION CELL INDEX (KI-67) OBTAINED BY EUS-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA)

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**Introduction:** PNET have been increasingly detected by imaging methods as computerized tomography (CT), magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS). The EUS-FNA could be an important tool to assess the prognostic factor in this disease through the determination of Ki-67, especially on a small PNET (< 3.0 cm) where management is still controversial.
**Aims & Methods:** To determine the natural history of PNET smaller than 3.0 cm managed conservatively and the role of Ki-67 in this case. From January 2010 to April 2015, 29 patients with histologically proven PNET were followed by MRI, CT and/or EUS. 19 were operated (Group 1) and 10 are being observed until the present day (Group 2).
**Results:** From the 29 patients studied, 23 (93%) were well differentiated PNET (Grade I – GI) and 2 (7%) were poorly differentiated neuroendocrine tumor (Grade II – GII). There was no statistical difference between groups regarding sex, mean age, symptoms and the localization of the PNET (head 13, body 14 and tail 2). The average size was of 1.5 cm (0.4–2.8 cm). EUS-FNA obtained sufficient material for Ki-67 in 18 patients (94.7%) of group 1 and 9 (90%) of group 2. Ki-67 was positive and < 5% in all cases of group 1 and in all but 1 patient from group 2 (patient with GII PNET). On group 1 there was 1 perioperative death (5.2%), 1 liver metastases (5.2%) which was resected after 24 months, and 17 (89.6%) kept without recurrence. In group 2, there was 1 liver metastasis (10%), 4 maintained hypoglycemic attacks (40%), 1 had tumor growth (10%) of 1.4 to 2.5 cm, being operated lately and 5 kept asymptomatic (50%). The mean tumor growth rate was 0.25 cm per year and no predictive factor of worse outcome was identified.
**Conclusion:** Conservative management of PNET smaller than 3.0 cm was safe. A Ki-67 < 5%, obtained by EUS-FNA on PNET was a reliable approach to choose the treatment strategy on this study. Prospective and larger multicenter studies with long-term follow-up are needed to validate this result.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0662 THE ROLE OF EUS-FNA IN THE DIAGNOSIS AND GRADING OF PANCREATIC NEUROENDOCRINE TUMORS

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**Introduction:** One of the most controversial issue in the diagnosis of pancreatic neuroendocrine tumors (pNET) is the accurate prediction of their clinical behaviour. The grading has to be expressed by using the mitotic index and the Ki67 proliferation index.
**Aims & Methods:** The aim of this study was to evaluate the role of the endoscopic ultrasound (EUS) fine needle aspiration (FNA) in the diagnosis and grading of pNET.
**Methods**: We retrospectively reviewed all consecutive patients with a radiological finding suspicious for pNET. A computerized system was used to extrapolate the list of patients between May 2014 and April 2016. In the present study, only patients with FNA were included. FNA was performed with Beacon or Boston Scientific 25 G or 22 G needles. In case of pathological diagnosis different from NET, the patient was excluded from analysis. Adequacy of the aspirated material was assessed by rapid on site evaluation. If any fragment was observed on the slide at macroscopic evaluation, it was placed into formalin for histology evaluation. In patients undergoing surgery the EUS-FNA results were compared with final histological diagnosis.
**Results:** 51 patients undergoing EUS were identified with 38 having also an FNA. Three pts were excluded because the NET was not confirmed after EUS–FNA: one patient had a SPT, one had a SCA, one had a metastasis from renal cancer. Study population included 35 patients: 15 female and 20 male, mean age 59 years (SD 13.6 y). Twenty-five patients (71.4%) had an incidental finding of pancreatic mass, 3 (8.6%) had genetic syndrome, 6 (17.1%) had symptoms like pain, weight loss or jaundice. One case (2.9%) was functioning NET (hypoglycemia). Clinical and technical data are summarized in the Table. The mean size of punctured lesions was 20 mm (SD 13.7) and the localization was the body and tail in 24 patients (68%), neck in 3 (8.6%), head in 3 (8.6%), uncinated process in 5 (14.3%). The 25-G needle was used in 28 patients (80%). The mean number of passages was 1,6 (SD 0.7; range 1–4). In 4 cases a mild self-limited bleeding was observed: one in a solid lesion, one in a solid-cystic lesion, one in a cystic lesion, and one into the pancreatic duct after FNA of a solid lesion infiltrating the pancreatic duct wall. The overall FNA adequacy was 97.1%. One inadequate case was that one with a mild bleeding in which the specimen was too bloody for pathological examination. The ki67 index was obtained in 25 cases (71.4%). Fourteen of 35 patients with pNET (40%) underwent surgery, one patient is waiting for surgery; 2 had chemotherapy; 18 are in follow up. The concordance rate between EUS-FNA grading and the grading on surgical specimen was 85.7% (12 of 14 patients). In two cases an up-grading was observed in the surgical specimen (from G1 to G2, because of a final ki67 of 3% compared to 2% in the FNA).
**Conclusion:** This study has some limitations mainly because of the retrospective design and the lack of histological examination on all FNA specimens. On the other hand, this study confirmed the high accuracy of the EUS-FNA in the diagnosis of pNET and the ability to evaluate the ki67 index on EUS-FNA cytology or histology material.

**Table (P0662)**

| Case n° | sex | age | Location | Size (mm) | n° passes | needle G | Features | Complications | Cytology | cytology ki67 | Histology | Histology ki67 | Final FNA adequacy | Surgery | Surgery ki67 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 72 | tail | 28 | 1 | 22 | N | N | Inadequate | NA | NET | <1% | Y | NET | 1% |
| 2 | M | 57 | tail | 16 | 1 | 25 | N | N | NET | <5% | NP | | Y | NET | 7% |
| 3 | F | 64 | neck | 15 | 2 | 25 | N | N | NET | NA | NP | | Y | NET | <2% |
| 4 | M | 68 | un proc | 18 | 1 | 25 | N | N | NET | NA | blood | | Y | NET | 13% |
| 5 | M | 71 | body | 11 | 2 | 25 | N | N | NP | | NET | <1% | Y | | |
| 6 | F | 56 | body | 12 | 4 | 25 | N | N | NET | NA | NET | <1% | Y | | |
| 7 | F | 39 | tail | 10 | 2 | 25 | N | N | NET | 10% | NP | | Y | NET | 2% |
| 8 | F | 61 | body | 7 | 1 | 22 | N | N | NET | NA | NET | <1% | Y | | |
| 9 | M | 46 | body | 24 | 2 | 25 | N | N | NET | NA | NET | <1% | Y | NET | 1% |
| 10 | F | 24 | un proc | 38 | 2 | 25 | Y | N | NET | NA | NET | 2% | Y | | |
| 11 | M | 69 | un proc | 50 | 2 | 22 | Y | N | CTM | NA | CTM | 30% | Y | | |
| 12 | M | 75 | un proc | 11 | 2 | 25 | N | N | NET | NA | NET | 1% | Y | | |
| 13 | F | 70 | tail | 9 | 1 | 25 | N | bleeding | Inadequate | | NP | | N | | |
| 14 | M | 69 | tail | 12 | 3 | 25 | N | N | NET | NA | NP | | Y | NET | |
| 15 | M | 36 | un proc | 11 | 1 | 25 | N | N | NET | NA | NET | 2% | Y | | |
| 16 | M | 72 | tail | 20 | 1 | 25 | N | N | NET | NA | NP | | Y | | |
| 17 | M | 66 | head | 20 | 1 | 25 | Y | N | NET | <1% | NP | | Y | NET | <1% |
| 18 | F | 44 | head | 53 | 2 | 22 | Y | N | NET | NA | NET | 4% | Y | NET | 7% |
| 19 | F | 52 | tail | 15 | 2 | 25 | Y | N | NET | NA | NET | <1% | Y | NET | 1% |
| 20 | M | 67 | tail | 22 | 1 | 25 | Y | N | NET | NA | NP | | Y | | |
| 21 | M | 45 | tail | 50 | 2 | 25 | N | N | NET | NA | NET | 8% | Y | NET | 14% |
| 22 | F | 47 | body | 8 | 2 | 25 | N | N | NET | NA | NET | NA | Y | | |
| 23 | F | 77 | body | 25 | 1 | 25 | N | N | NET | NA | NET | <1% | Y | | |
| 24 | M | 69 | body | 18 | 2 | 25 | Y | N | NET | NA | NET | NA | Y | | |
| 25 | M | 45 | body | 9 | 1 | 25 | N | N | NET | 5% | NP | | Y | | |
| 26 | M | 65 | body | 12 | 1 | 22 | Y | bleeding | NET | NA | NET | <1% | Y | NET | 1% |
| 27 | F | 64 | head | 34 | 2 | 22 | N | N | NET | NA | NET | 2% | Y | NET | 3% |
| 28 | F | 61 | body | 7.5 | 1 | 25 | N | N | NET | NA | NET | 2% | Y | | |
| 29 | M | 60 | neck | 12 | 2 | 25 | N | N | NET | NA | NP | | y | | |
| 30 | m | 58 | tail | 23 | 1 | 22 | Y | N | NET | NA | NP | | y | Waiting for | |
| 31 | M | 76 | neck | 8 | 1 | 25 | N | EndoW blee | NET | NA | NET | 2% | Y | | |
| 32 | M | 63 | body | 50 | 2 | 25 | Y | N | NET | NA | NET | 5% | Y | | |
| 33 | F | 71 | body | 9 | 1 | 25 | N | N | NET | NA | NET | 1% | Y | | |
| 34 | M | 30 | tail | 9 | 1 | 25 | N | N | Inadequate | NA | NET | 2% | Y | NET | 3% |
| 35 | F | 70 | body | 9 | 1 | 25 | Y | N | NET | NA | NET | <1% | Y | | |

**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00

**ENDOSCOPY AND IMAGING II – POSTER EXHIBITION**

### P0663 SIMPLE AND SAFE FORCEP STRIP TECHNIQUE FOR GASTRIC SUBMUCOSAL TUMORS ORIGINATING FROM MUSCULARIS PROPRIA LAYER

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**Introduction:** Resection of submucosal tumors by means of endoscopy has been reported using a variety of techniques. However, lesions originating from the pro-pria muscle layer are unlikely to be re-sected completely and safely.

**Aims & Methods:** Here, we report the first series describing the new technique of endoscopic resection for submucosal tumors of the stomach using the simple and safe forcep strip technique. Endoscopic submucosal tumor resection using hot biopsy forcep was attempted in ten consecutive patients in clinical indications for lesion removal. Following injection around the submucosal tumor, the adjacent mucosa or submucosa was grasped with the forceps and pulled away forming a "tent". Electrocoagulating current was applied for dissection of tissue. For repeating described process, the tumor was dissected from the muscularis propria layer and then carefully removed using forcep.

**Results:** All of the ten patients that underwent Forcep Strip Technique for the gastric submucosal tumors were successful, with the complete resection rate of 100%. There was no major bleeding and the procedure time was reduced compared to the conventional methods. No complications occurred and follow-up was unremarkable. It is possible to resect submucosal tumor any part of the stomach (fundus, cardia, body). On histology, all tumors were resected completely (eight gastrointestinal stromal tumor, two leiomyomas).

**Conclusion:** Forcep Strip Method appears to be an easy, safe, and effective procedure for treatment of gastric submucosal tumor originating from the muscularis propria layer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0664 MINIMAL ESOPHAGEAL LESIONS DETECTED BY DIGITAL CHROMOENDOSCOPY USING OPTICAL ENHANCEMENT SYSTEM™ ASSOCIATED TO HIGH DEFINITION PLUS OPTICAL MAGNIFICATION IN NON EROSIVE REFLUX DISEASE (NERD)

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**Introduction:** Patients with gastroesophageal reflux disease (GERD) have an increased number, dilation and tortuosity of the microscopic intra-papillary capillary loops (IPCLs). Recently, an image-enhanced technology called Optical Enhancement system (OE system™) is equipped in Pentax video processor EPK-i7010. It improves visualization of microvessels. Also new high-definition scopes with optical magnification (Magniview™) were developed. The scopes increase the image up to 136 times with a better evaluation of the mucosa.

**Aims & Methods:** To evaluate the diagnosis ability of OE system™ +Magniview™ scopes, to detect minimal esophageal lesions (MEL) (IPCLs) and predict reflux in non-erosive reflux disease (NERD) patients. Methods: Prospective, non-randomized, simple blind study. Patients enrolled had typical GERD symptoms. If esophagus was normal at endoscopy, a pH-impedanciometry was performed to discriminate NERD patients (NG) from non reflux disease (Control group [CG]). Finally an OE system™ +Magniview™ endoscopy was performed. Images were recorded and examined blindly by 3 endoscopists. Biopsies from each esophagus level were done. Images were compared to histology to predict inflammation. Inclusion Criteria: >18 years-old, agree to participate, GERD symptoms (>8 points at GERD questionnaire), absence of Barrett's esophagus or erosive sign (Los Angeles classification: Grade A-D) by

**Table. (P0664):** Contingency Table comparing Upper Endoscopy with Ph-Impedanciometry and histopathological Biopsy

| | Sensitivity % (95% IC) | Specificity % (95% IC) | PPV % (95% IC) | NPV % (95% IC) | Accuracy % |
|---|---|---|---|---|---|
| PH-IMPEDANCIOMETRY | | | | | |
| UE lower third | 88.89 (73.94 – 96.89) | 85.71 (63.66 – 96.95) | 91.43 (76.94 – 98.20) | 81.82 (59.72 – 94.81) | 87.72 |
| UE middle third | 75.00 (57.80 – 87.88) | 62.50 (40.59 – 81.20) | 75.00 (57.80 – 87.88) | 62.50 (40.59 – 81.20) | 73.68 |
| UE upper third | 80.56 (63.98 – 91.81) | 66.67 (43.03 – 85.41) | 80.56 (63.98 – 91.81) | 66.67 (43.03 – 85.41) | 75.44 |
| UE in general | 94.44 (81.34 – 99.32) | 61.90 (38.44 – 81.89) | 80.95 (65.88 – 91.40) | 86.67 (59.54 – 98.34) | 82.46 |
| BIOPSY | | | | | |
| UE lower third | 92.31 (74.87 – 99.05) | 64.52 (45.37 – 80.77) | 68.57 (50.71 – 83.15) | 90.91 (70.84 – 98.88) | 77.19 |
| UE middle third | 81.82 (59.72 – 94.81) | 57.14 (39.35 – 73.68) | 54.55 (36.35 – 71.89) | 83.33 (62.62 – 95.26) | 66.67 |
| UE upper third | 89.47 (66.86 – 98.70) | 50.00 (33.38 – 66.62) | 47.22 (30.41 – 64.51) | 90.48 (69.62 – 98.83) | 63.16 |
| UE in general | 96.55 (82.24 – 99.91) | 50.00 (30.65 – 69.35) | 66.67 (50.45 – 80.43) | 93.33 (68.05 – 99.83) | 73.68 |

endoscopy (by neither white light nor I-Scan™). Exclusion Criteria: Barrett's esophagus or erosive sign (Los Angeles classification), history of esophagitis, achalasia, esophageal varices, esophageal cancer, PPI or NSAIDs consumption, coagulopathy, gastric lesions, gastroparesis, history of esophageal/gastric surgery, pregnancy, lactation.
**Results:** 57 patients were analyzed [36 (63.15%) NG, 21 (36.85%) CG] [mean age 48 years old, 46 women (81%)]. The main symptom was regurgitation in 27 cases (47.3%). IPCLs was observed in 94.4% of NG, being the lower third the most affected ($p < 0.05$). In CG 8 patients (38%) had IPCLs ($p < 0.05$ for NG). The IPCLs dilatation was the most common find (91.6%). Unlike IPCLs tortuosity, both dilatation and increased number of IPCLs showed a significant difference between groups. Also both lesions were more common ($p < 0.05$) between patients with inflammation at histology. The ability to predict GERD with OE system™ +Magniview scopes was determined/compared with Ph-Impedanciometry (gold standard). The sensitivity, specificity, PPV, NPV and accuracy was 94.4%, 61.9%, 91.4%, 81.8% and 86.67% respectively. The lower third of the esophagus had the higher sensibility and accuracy (88.9% and 87.72). The Kappa inter and intra-observer value was 0.85 and 0.90 respectively.
**Conclusion:** OE system™+Magniview™ scopes can detect MEL and predict GERD with a high sensitivity and accuracy. The presence of MEL has a high grade of correlation with a histology inflammation.
ClinicalTrials.gov Identifier: NCT02575287
**Disclosure of Interest:** C. Robles-Medranda: Key Opinión Leader for Pentax Medical
All other authors have declared no conflicts of interest.

## P0665 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS WITH THE CONTINUOUS USE OF LOW-DOSE ASPIRIN: ANALYSIS OF 101 PATIENTS

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**Introduction:** Although the safety of endoscopic submucosal dissection (ESD) for gastric neoplasms has been established, the postoperative bleeding after ESD is one of the major complication. Low-dose aspirin (LDA) is usually used for the prevention for cardiovascular and cerebrovascular diseases. Reportedly, the continuous use of LDA (continued-LDA) seems to be a high risk for bleeding after endoscopic treatment. Guidelines recommend that high risk bleeding endoscopic procedures including gastric ESD are not required to discontinue LDA in patients with a high risk for thrombosis whereas LDA should be discontinued in patients with a low risk for thrombosis. Recent retrospective studies have been described that continued-LDA has not significantly increased postoperative bleeding after gastric ESD compared with discontinued-LDA. However, there has been a limitation, such as small samples. We treated with gastric ESD in 101 patients with continued-LDA and assessed the postoperative bleeding and clinical outcomes compared with discontinued-LDA.
**Aims & Methods:** A total of 480 patients who underwent ESD for gastric neoplasms at the New Tokyo Hospital between August 2008 and October 2015 were enrolled in this study. We categorized patients into three groups: continued-LDA (100 mg/day, n = 101), discontinued-LDA for 5 days or more (n = 46), and without LDA intake (control, n = 333). Multivariate analyses were performed to analyze the differential effect of continued-LDA and discontinued-LDA on postoperative bleeding.
**Results:** The postoperative bleeding occurred in 6.9% (33/480) overall, and in 4.2% (14/333) in the control group. The postoperative bleeding rate in the continued-LDA group was observed to be lower than in the discontinued-LDA group (11.9% [12/101] versus 15.2% [7/46]), but no significant differences were found between the two groups on logistic regression analysis (OR, 1.33; 95% CI 0.49–3.64). Multiple logistic regression analysis showed that no significant differences in postoperative bleeding were found between the two groups (OR, 1.20; 95% CI 0.43–3.36).

**Table:** Logistic regression analysis for postoperative bleeding after gastric ESD between continued-LDA and discontinued-LDA

| | Postoperative bleeding (n = 19) | Non postoperative bleeding (n = 128) | Odds ratio | 95%CI | P value |
|---|---|---|---|---|---|
| LDA, n (%) | | | | | |
| Discontinued | 7(15.2) | 39(84.8) | 1.33 | 0.49–3.64 | 0.58 |
| Continued | 12(11.9) | 89(88.1) | reference | | |

ESD, endoscopic submucosal dissection; LDA, low-dose aspirin; CI, confidence interval.

**Conclusion:** The continuous use of LDA was not an increase for the risk of postoperative bleeding compared with interruption of LDA. The continuous use of LDA is applicable to gastric ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0666 A NOVEL FULLY SYNTHETIC AND SELF-ASSEMBLED PEPTIDE SOLUTION FOR ENDOSCOPIC SUBMUCOSAL DISSECTION INDUCED ULCER; A FEASIBILITY STUDY

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**Introduction:** Endoscopic submucosal dissection (ESD) can remove varying size early stage gastrointestinal tumors en bloc, however, delayed bleeding can occur days after the procedure and success requires reducing a relatively high post-procedure bleeding rate; 1% esophagus, 4.6 to 15.6% stomach and 2.0 to 2.5% colorectum. Gastric ESD-induced ulcers are treated with proton pump inhibitor for at least 8 weeks after ESD in most hospitals. Recently, tissue engineering and regenerative substances have been developed to target the reconstruction of structurally and functionally normal tissues.
**Aims & Methods:** The aim of this study was to assess the safety and efficacy of a novel fully synthetic and self-assembled peptide solution which functions as an extracellular matrix scaffold material that facilitate the reconstruction of normal tissues (PuraMatrixTM, 3-D Matrix, Ltd, Tokyo, Japan) in ESD-induced ulcers. Consecutive patients who underwent esophageal, gastric and colorectal ESDs were prospectively enrolled. This solution was applied to the ESD-induced ulcer using a catheter immediately after the procedure. Post-ESD bleeding was defined as bleeding that required transfusion, endoscopic or surgical intervention, or bleeding that caused the hemoglobin level to fall by 2 g/dl in addition to changes in vital signs. Gastric ulcers were evaluated by

endoscopy and classified as active, healing or scarring stages at 1, 4 and 8 weeks after ESDs. The study endpoints were the rate of post-ESD bleeding, the transitional rate to healing and scarring stages of gastric ESD-induced ulcers.
**Results:** One hundred and twenty-two patients including 26 (21.3%) previously on antithrombotic therapy and 7 (5.7%) requiring heparin bridge therapy with 133 lesions were analyzed. The mean size of en bloc resected specimen was 40.6 ± 15.6 mm. The overall rate of post-ESD bleeding was 1.5% (2/133; 95%CI, 0.4–5.3). Bleeding from esophagus, stomach and colorectum were 0% (0/19), 2.0% (1/51) and 1.6% (1/63), respectively. Transitional rate to healing stage of ESD-induced ulcer at 1 week was 96% (49/51). Further follow up endoscopies demonstrated the scarring stage in 19% (9/48) and 98% (41/42) at 4 and 8 weeks, respectively. There were no adverse effects related with this solution.
**Conclusion:** This novel peptide solution can potentially aid in reducing the delayed bleeding rate by promoting mucosal regeneration and speed of ulcer healing after large mucosal and submucosal resections. Further studies are needed to fully evaluate its efficacy.
**Disclosure of Interest:** T. Uraoka: – No financial relationships relevant to this presentation. – This study was supported by Japan Society for the Promotion of Science of Grant-in-Aid for "Scientific Research (C)".
All other authors have declared no conflicts of interest.

## P0667 DETECTION OF EARLY NEOPLASIA AND PREDICTION OF TREATMENT EFFICACY FOR ADVANCED CANCERS USING HYPOXIA IMAGING ENDOSCOPY EQUIPPED WITH LASER SOURCE

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**Introduction:** Recent endoscopy has evolved into image-enhanced endoscopy (IEE), such as Narrow Band Imaging and Blue Light Imaging. IEE focused on increasing abnormal microvessels in the surface of early cancers. In contrast, hypoxia is one of the functional characteristics in cancer, with strong association to the biological features. The investigation of cancer hypoxia was started in the 1960's, with poor prognosis in hypoxia cases for chemotherapy or radiotherapy. In these many studies, polarographic needle electrodes for direct tumor-tissue were used as oxygen measurements. However, there has been no modality in which hypoxia imaging is visible in real-time and in the whole tumor. Therefore, hypoxia imaging was innovated to visualize directly the biological and functional changes in cancer.
**Aims & Methods:** The aim of this prospective study is to evaluate the visualization of whole feature in early cancers and to predict treatment efficacy for advanced cancers using hypoxia imaging endoscopy. In endoscopic equipment, we utilized a difference of absorption between oxy- and deoxy-hemoglobin in visible light wavelength. The signals converted from laser light were calculated in oxygen saturation (StO2) by processor. Hypoxia imaging was obtained in real-time, displaying two types of StO2 images. One was a pseudocolor image showing StO2 levels as different hues, and the other was an overlay image that overlapped low StO2 levels in blue on a white light illumination image of background mucosa. In the initial clinical trial, hypoxia imaging was analysed in early cancers and adenomas of the pharynx, esophagus, stomach, or colorectum. As the second trial, a prediction of treatment efficacy in advanced cancers of the esophagus, stomach, or colorectum using hypoxia imaging was evaluated between before and after chemotherapy. To compare histologic findings to hypoxia imaging, all patients with early-sided lesions received endoscopic resection immediately after conventional and hypoxia imaging endoscopy, and all patients with advanced cancers were histologically confirmed by biopsy. All lesions were evaluated the prediction of treatment efficacy in StO2 levels obtained from the StO2 map.
**Results:** Forty patients with early-sided lesions were analysed. The hypoxic area was completely corresponded to the portion of early cancer, with clearly visible in cancer edge. Furthermore, 8 colorectal low-grade adenomas were also detected as hypoxia, ranging from 3 to 10 mm in diameter. All esophageal cancers including 2 Barrett's cancers were detected in hypoxia images. Median StO2 differences between neoplastic and non-neoplastic areas in the pharynx, esophagus, stomach and colorectum were −15.4%, −14.5%, −5.1% and −21.5%, respectively. Significant differences of StO2 levels were seen in the esophagus ($p = 0.0078$, $n = 8$) and colorectum ($p = 0.0001$, $n = 14$), but not in the stomach ($p = 0.9341$, $n = 15$) or pharynx ($p = 0.2500$, $n = 3$). In the prediction of treatment efficacy in the 15 advanced esophageal, gastric and colorectal cancers, accuracy before chemotherapy and after 1 curse of individual chemotherapy was 62% and 92%, respectivery.
**Conclusion:** Hypoxia imaging with the laser endoscope enables us to visualize spatial and temporal information of hypoxic conditions in adenoma, early and advanced cancers. Hypoxia imaging illustrates a novel aspect of cancer biology as a potential biomarker and can be widely utilized in cancer diagnosis and prediction of treatment efficacy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0669 HANDS-ON TRAINING ON PORCINE MODELS FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) AND PER-ORAL ENDOSCOPICMYOTOMY (POEM) – DOES IT HELP TRAINING OF PHYSICIANS FOR THESE ADVANCED PROCEDURES?

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**Introduction:** Expertise in advanced endoscopy procedures – endoscopic submucosal dissection (ESD) and per-oral endoscopic myotomy (POEM) is largely limited to few select centers. A global need for trained physicians competent to perform these advanced endoscopy procedures has been identified. Optimum training in these procedures has been traditionally difficult to obtain due to limited opportunities and ethical issues regarding training on live patients. Our center has considerable experience in performing ESD and POEM and conducts regular endoscopy training programs. We developed a special fresh cadaver porcine model for ESD and POEM training at our center. During a 12-month period, four hands on ESD and POEM training workshops using this model were conducted. Participants were endoscopists with more than 5 years' experience in advanced therapeutic endoscopy including ERCP. This study aims to evaluate the impact of these training courses amongst the participants and their subsequent clinical practices.
**Aims & Methods:** 116 endoscopists participated in a 2-day ESD / POEM workshop with hands on training on specially developed porcine models over 4 training courses conducted over a 12-month period. All participants completed a detailed feedback form at end of the course wherein they had to mention if they would perform these procedures within 6-months. Each physician was contacted by telephonic survey 8-months after the workshop. The questionnaire evaluated the following points – whether they had initiated any of the procedures – ESD or POEM, reason for noninitiation, type of procedure initiated, number of procedures performed to date, difficulties faced during procedure, desire to attend further similar workshops.
**Results:** Of 116 participants, 102 responded via feedback form were inclined to perform these procedures within 6-months. Of these, 88 participants (75.8%) could be contacted for the post workshop telephonic survey. 23/88 (26.1%) confirmed having attempted and 22/88 (25%) successfully performed either ESD or POEM within 6-months. ESD was performed by 15 (17%), POEM by 4 (4.5%) and both ESD & POEM by 3 (3.4%) physicians. No significant adverse events were reported. Amongst 65 physicians who did not initiate any procedure, 40 (61.5%) cited lack of instrumentation and infrastructure as the reason, 9 (13.8%) mentioned lack of suitable patients whereas 12 (18.4%) physicians requested additional hands-on training prior to initiation.
**Conclusion:** The current study shows a significant impact of hands-on training models with 25% participants initiating ESD and POEM. Only 18% participants requested additional training before initiating these procedures. Hands-on training workshops on specially developed fresh cadaveric porcine models may serve as an important platform for aspiring endoscopists who wish to train in these advanced procedures.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0670 PRAGUE CLASSIFICATION FOR BARRETTES OESOPHAGUS: A STUDY TO SEE THE DEGREE OF COMPLIANCE BY THE ENDOSCOPISTS

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**Introduction:** The British Society of Gastroenterology (BSG) guidelines on Barrettes oesophagus were modified in 2015. Firstly, the guidelines focus on precise documentation of the findings. The Prague Classification has been recommended as a standard. This takes into account the circumferential extent (C) as well as the maximal longitudinal extent (M) of the Barrettes segment as measured from the gastro-oesophageal junction. It is therefore called the "Prague CM classification". Secondly, the guidelines have focused on presence or absence of any histological intestinal metaplasia and/or dysplasia in relation to the length of Barrettes segment. This study aims at finding the compliance rate of endoscopists to Prague CM classification for reporting of Barrettes oesophagus. This study focuses only on the first aspect of the guidelines regarding diagnosis of Barrettes oesophagus, as the second aspect (interval surveillance endoscopy) depends on the first after histology is incorporated into the information.
**Aims & Methods:** This is a retrospective study recruiting all the cases who were documented in the endoscopy reports as "Barrettes Oesophagus" upon having gastroscopy in a sample district general hospital of United Kingdom between January 2014 and May 2015. All new and old diagnosis of Barrettes oesophagus in the period of 18 month were included in this study. Endoscopy reports from all professionals doing the upper GI endoscopy in this sample unit were included in the study. Therefore there were reports from the Consultant Gastroenterologists, Consultant Surgeons, Registrars and Nurse Endoscopists included in the study. Data was retrieved from hospital computer records and individual report was analysed in detail.
**Results:** There were 39 patients who had endoscopy and were recorded with a definitive diagnosis of Barrettes Oesophagus. Only 18 (46%) of these had been documented using the Prague CM classification and 21(54%) had no such documentation. In the unit 19 (48.8%) of GI endoscopy was done by the Consultants, 6 (15.3%) by Registrars and 14 (35.9%) by the Nurse Practitioners. When analysis was made based upon the operator, it was seen that 63% of Consultants, 33% of Registrars and 50% of the nurses did not

document Barrettes oesophagus using the Prague CM classification. It is clear that the registrars have done better than the consultants or nurse practitioners in adhering with the guidelines.
**Conclusion:** Our study has shown lack of adherence with BSG guidelines on documentation of Barrettes Oesophagus using Prague CM classification in a sample district general hospital of United Kingdom over a period of 18 months consistently. Whereas the sample represents practice in one district only, more studies are required to see what is happening in other districts. Some possible causes for poor documentation can be; time constraints during busy endoscopy lists, lack of knowledge about the Prague CM classification, not being convinced about the value of using the classification, lack of IT support in the form of endoscopy reporting tool which may not have built in provision for using the classification or simply that the operator could not be bothered. This study has also shown better adherence to the guidelines on documentation by the registrars in comparison to the consultants and the experienced nurse practitioners. Possible causes for this can be; new training techniques in endoscopy which the registrars are more likely to have received recently, In any case the use of Prague CM classification to describe Barrettes Oesophagus has multiple advantages. For example, it enables better planning of interval for surveillance endoscopy. If the segment is below 1 cm in size and there is no histological metaplasia or dysplasia, endoscopy has to be repeated once only. If same findings are seen then patients can be discharged from the surveillance program. If it is more than 3 cms in size, then repeat endoscopy is recommended based upon histological presence or absence of intestinal metaplasia and/or dysplasia. Furthermore the classification enables operator to estimate progression or regression of Barrettes. It also enables a validated universal understanding of the extent of the disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0671 RISK FACTORS FOR METACHRONOUS GASTRIC CARCINOMA DEVELOPMENT AFTER ENDOSCOPIC RESECTION OF GASTRIC DYSPLASIA; RETROSPECTIVE, SINGLE CENTER STUDY

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**Introduction:** Gastric dysplasia is a known precursor lesion of invasive adenocarcinoma, so endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is routinely performed to remove this premalignant lesion. Upon removal of the dysplasia, gastric adenocarcinoma (GAC) can be detected during the follow-up period, but few studies have addressed the factors related to gastric cancer occurrence.
**Aims & Methods:** We determined the occurrence rate of GAC and related factors by evaluating the follow-up results of patients who had been confirmed with gastric dysplasia after endoscopic resection. We retrospectively analyzed the medical records, endoscopic examination records, endoscopic procedure records, and histological records for 667 cases in 641 patients being followed up over 1 year, among the 1,273 patients who had been confirmed with gastric dysplasia after EMR or ESD for gastric mucosal lesions between January 2007 and August 2013at the Chungnam National University Hospital.
**Results:** The mean follow-up period was 33.8 months and the median follow-up period was 29 months (range, 12–87). During the follow-up period, the occurrence of metachronous GAC was 4.0% (27/667). The mean and median interval periods between occurrence of metachronous GAC and endoscopic treatment of GA were 36.3 months and 34 months, respectively (range, 16–71). The factors related to metachronous GAC occurrence after endoscopic resection for gastric dysplasia were male sex (5.3% vs. 1.0%), open type of atrophic gastritis (9.5% vs. 3.4%), intestinal metaplasia (6.8% vs. 2.4%), and high grade dysplasia (8.4% vs. 3.2%). Among these, male sex [OR: 5.05 (1.18–21.68) $p = 0.029$], intestinal metaplasia [OR: 2.78 (1.24–6.23) $p = 0.013$], and high grade dysplasia [OR: 2.70, (1.16–6.26) $p = 0.021$] were independent related factors in a multivariate analysis. Among the 27 GAC cases, 24 cases (88.9%) occurred at locations other than the previous resection sites and 3 cases (11.1%) occurred at the same locations as the previous resection sites.
**Conclusion:** Male sex, intestinal metaplasia, and high grade dysplasia were significantly related to the occurrence of metachronous GAC after EMR/ESD for gastric dysplasia, and most cases occurred at locations other than the previous resection sites.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0672 DOES SHOCK INDEX (SI) CONTRIBUTE IN THE RISK ASSESSMENT OF PATIENTS WITH ACUTE UPPER GASTROINTESTINAL BLEED (AUGIB)?

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**Introduction:** Patients presenting with acute upper gastrointestinal bleeding (AUGIB) are risk assessed by calculating pre-endoscopy Rockall score (RS). Shock index (SI) [ratio between highest heart rate (HR) and lowest systolic blood pressure (SBP) has been described as an easy-to-use clinical tool that rapidly identifies patients at risk of haemodynamic decompensation (NCEPOD report)[1]. We have shown previously that RS is inaccurately documented in 78% cases[2]. The aim of this study was to compare SI with RS in patients with AUGIB. RS of $<3$ was considered low risk, while $>3$ as moderate to high risk. SI $<0.7$ was taken as low risk and $>0.7$ as moderate to high risk.
**Aims & Methods:** A retrospective analysis was conducted for all patients with AUGIB from January to December 2015 at Croydon University Hospital. Copies of electronic referral forms and endoscopy reports were scrutinised. RS was ascertained from the electronic endoscopy request form while SI was determined by scrutinizing patient observations. Endoscopic findings and therapeutic interventions were also recorded.
**Results:** Of the 195 patients, 123(63%) were male. Presenting symptom was haematemesis including coffee ground vomiting in 85 (44%) patients, melaena in 95(49%), PR bleeding in 15(8%) patients. In 152(78%) patients gastroscopy was performed within 24 hours, 27(14%) between 24–48 hours, 10(5%) in 48–72 hours and 6(3%) $>72$ hours. Endoscopy was abnormal in 144 patients (75%) which included peptic ulcer in 79 patients (55%), varices in 14 (10%), vascular lesions in 7(5%), malignancy in 3, Mallory Weiss tear in 2 and mild inflammation in 41(28%) patients. 143(73%) patients required no endoscopic intervention. Of the remaining 52 patients, variceal banding was performed in 6(3%) patients, adrenaline and endoclips in 9(5%), adrenaline and gold probe in 29 (15%) and APC done in 8 (4%) patients. SI was $<0.7$ in 67(34%) and $>0.7$ in 128(66%) patients. RS was $<3$ in 77(39%) and $>3$ in 118(61%) patients. Endoscopic intervention was required in 3 of 42 patients(7%) with RS $<3$ and SI $<0.7$, 5 of 54 patients(9%) with RS $>3$ and SI $<0.7$, 30 of 50 patients(60%) with RS $>3$ and SI $>0.7$ and 14 of 49 patients(28%) with RS $<3$ and SI of $>0.7$ required treatment. For predicting likelihood of applying endoscopic therapy for AUGIBs, RS $>3$ had a sensitivity of 67%, specificity of 37%, positive predictive value of 35% and a negative predictive value of 69%. SI $>0.7$ had a sensitivity of 84%, specificity of 61%, positive predictive value of 44% and negative predictive value of 91%.
**Conclusion:** This study shows that shock index more accurately predicts the likelihood of a patient with AUGIB requiring endoscopic intervention. SI had a higher sensitivity, specificity, negative and positive predictive value compared to RS. SI indicated a high risk GI bleed in 28% patients who were triaged as low risk bleed on pre-endoscopy RS alone. Limitation of this study is the accuracy of RS documentation which could have affected the comparison.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0673 CREATING A VIRTUAL LESION WITH A POLYPECTOMY SNARE: A SIMPLE AND INEXPENSIVE METHOD TO ASSESS THE "PIG R0 RESECTION RATE" DURING ENDOSCOPIC SUBMUCOSAL DISSECTION TRAINING IN ANIMAL MODELS

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**Introduction:** Animal models have proven efficacious for overcoming the ESD learning curve with satisfactory results and are recommended in western countries because of a lack of recruitment due to epidemiological differences and the lack of available experts to help with hands-on learning and training. Only en-bloc but not R0 resection rates have been evaluated in all animal model studies because a measurable virtual lesion is lacking
**Patients & Methods:** From March 2013 to April 2016 we performed a retrospective analysis of prospective collected data. 73 virtual standardised gastric lesions were resected by ESD. There were created by applying an open polypectomy snare on the gastric mucosa using a soft coagulation current (effect 5) during 3 s. Primary outcome was the evaluability of the specimen that was considered assessable if the virtual lesion was clearly visible during and at the end of the procedure. Pig R0 resection was defined by macroscopic visualization of the entire snare scar on the specimen with a 1 mm macroscopic margin.
**Results:** The creation of the virtual lesions was feasible in 100% of cases. The specimens were assessable in 100% of cases and the lateral margins were easily measured in 100% of cases. The marks around the virtual lesion were visible at

the end of the procedure in 44 specimens (60%) but in 35 (79.5%) cases the marks were considered less visible than the virtual lesion. 63 (86.3%) were considered "R0" resected.
**Conclusion:** After initially learning the technique, one of the most challenging aspects for the endoscopist is to perform a complete resection of a human lesion. ESD is performed after coarsely marking the lesion while learning on an animal model. Then the en bloc resection rate is evaluated but not the R0 resection rate, particularly when the marks are not visible, as in 35% of our cases. The en bloc resection rate is not an actual solid primary outcome, whereas the R0 resection rate is the final goal of ESD. Moreover, this virtual lesion allows the trainee to learn all steps of the procedure including marking around the lesion. The size of the virtual lesion is easily adaptable using different sizes of polypectomy snare, which can be applied in different locations of the pig stomach.
**Conclusion:** Creating a virtual lesion with an open polypectomy snare and a soft coagulation current is an easy, cheap, and reproducible method effective in 100% of cases. That adds the possibility of reliably evaluating the pig R0 resection rate without need of a pathological analysis that could be very useful during ESD training and research. We could imagine a threshold of pig R0 resection rate that would be defined for different locations according to difficulty before a trainee would be considered effective enough to begin human ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0674 TARGETED BIOPSY UNDER GUIDANCE OF MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING MAY BE NOT NECESSARY WHEN COMBINED WITH MAGNIFYING ENDOSCOPY WITH NARROW BAND IMAGING: A PROSPECTIVE DIAGNOSTIC ACCURACY STUDY


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**Introduction:** Endoscopic forceps biopsy (EFB) is considered the gold standard and most commonly used for histological diagnosis of gastric cancerous lesions before proper management, however, with considerable discrepancy rate of 27.1–44.5% with final resected specimen. With advancement of endoscopic techniques, magnifying endoscopy with narrow band imaging (ME-NBI) has been widely used in diagnosis of cancerous lesions with relatively high diagnostic efficacy. Different from application of ME-NBI in the esophagus and colorectum, consolidated standard haven't been established for diagnosis of gastric cancerous lesions and there are many diagnostic standard proposed such as MSVS, which was most commonly used. Besides, compared with cancerous lesions in the esophagus and colorectum, high-grade intraepithelial neoplasia (HGIN) even early gastric cancer (EGC) are the most difficult to be subjectively evaluated and diagnosed using ME-NBI. Thus, diagnostic efficacy differed significantly between endoscopists even in Japan [1]. Therefore, for endoscopists especially novice endoscopists, it is common and seems reliable to perform targeted biopsy under guidance of ME-NBI (MNTB) when they were not sure for diagnosis of cancerous lesions using ME-NBI. Actually, studies have shown that MNTB has better diagnostic performance than EFB.
**Aims & Methods:** The aims of this study were to validate diagnostic efficacy of targeted biopsy under guidance of ME-NBI (MNTB) and further evaluate whether it is necessary to perform MNTB when combined with ME-NBI using MSVS diagnostic criteria [2] with a minor adjustment. This study prospectively analyzed 211 gastric lesions suspected of cancerous lesions. gastric lesions were classified as ME-NBI (+) (Definite cancer), ME-NBI (Suspected) (Indefinite but suspected cancer), ME-NBI (-) (Definite non-cancer). After careful observation under ME-NBI view, MNTB would be performed where abnormal or suspiciously abnormal features were observed. If no abnormal structures were detected, biopsy would be performed on the depressed area of gastric lesions or within the demarcation line of lesions. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of EFB, ME-NBI, MNTB, EFB plus ME-NBI, MNTB plus ME-NBI for diagnosis of cancerous lesions were determined respectively. Accuracy, sensitivity, specificity of EFB and MNTB, EFB plus ME-NBI and MNTB plus ME-NBI were also compared respectively.
**Results:** The accuracy, sensitivity and specificity with 95% confidence intervals were 68.2% (61.4–74.4%), 62.3% (54.1–69.9%), 84.2% (71.6–92.1%) for EFB, 75.4% (68.9–80.9%), 72.7% (64.9–79.4%), 82.5% (69.6–90.8%) for MNTB, 76.8% (70.4–82.2%),73.4% (65.5–80.0%), 86.0% (73.7–93.3%) for ME-NBI, 82.0% (76.0–86.8%), 85.7% (79.0–90.6%), 71.9% (58.3–82.6%) for EFB plus ME-NBI, 84.8% (79.1–89.3%), 89.6% (83.4–93.8%), 71.9% (58.3–82.6%) for MNTB plus ME-NBI respectively. The sensitivity of MNTB was significantly higher than EFB ($P = 0.048$). There was no significant difference in the sensitivity ($P = 0.307$), specificity ($P = 1.000$) and accuracy ($P = 0.337$) between EFB plus ME-NBI and MNTB plus ME-NBI.
**Conclusion:** Though MNTB had higher diagnostic efficacy than EFB in diagnosis of cancerous lesions, it may be not necessary to perform MNTB when combined with ME-NBI. MNTB didn't show better diagnostic performance than EFB in the group of suspected cancerous lesions under ME-NBI. Our study showed that it should arrest our attention because MNTB don't boost cost-effectiveness in diagnosing gastric cancerous lesions and even increase unnecessary waste of medical resources. When we're not sure for diagnosis of cancerous lesions using ME-NBI, we could use the former EFB pathology and endoscopic features to diagnose cancerous lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0675 AUTOMATIC LABELING OF ABNORMAL MICROVESSELS ON EARLY GASTRIC CANCER: MAGNIFYING NARROW-BAND IMAGING USING GRAY-LEVEL CO-OCCURRENCE MATRIX AND VECTOR QUANTIZATION TECHNIQUES


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**Introduction:** Magnifying narrow-band imaging (M-NBI) is useful in making endoscopic diagnosis of early gastric cancer (EGC). Evaluation of morphological feature of microvessels are key to make diagnosis of EGC in M-NBI, however, interpretation of microvessel patterns is often subjective and needs certain time to achieve expertise. In our project, we aim to develop computer-aided diagnosis (CAD) algorithms to reduce variation and to facilitate learning in interpreting microvessel patterns of EGC in M-NBI.
**Aims & Methods:** In this study, a hundred M-NBI images from 100 EGCs were prepared as a training set. We firstly pre-processed these images with histogram equalization and Gaussian filtering to enhance microvessels. Each image was divided into blocks of $40 \times 40$-pixels size and, for the each block, mean and standard deviation of the gray-level co-occurrence matrix (GLCM) parameter considering four directions were obtained [1]. Then, these GLCM data were defined as the feature vector of the specific image block and used for constructing a database of all defined feature vectors. To reduce the computational complexity, we clustered the feature vectors using the vector quantization (VQ) technique. The test set consisted of other 10 M-NBI images of EGC. An expert who has experience of $>1{,}000$ cases for M-NBI diagnosis delineated the area with irregular microvessels in the M-NBI images and this was served as reference standard. The same algorithms as in the training set were applied to the images in the test set, and the Euclidean distance of feature vectors between the each block in the test set and those in the database was calculated. When the Euclidean distance is less than a threshold value (0.15), the image block was diagnosed as abnormal. The microvessels within the abnormal areas were automatically colored using our previously developed microvessel labeling algorithms.
**Results:** Compared with the expert diagnosis (area_physician), our CAD (area_CAD) achieves the mean precision rate (area_physician area_CAD / area_CAD) of 75% and the mean recall rate (area_physician area_CAD / area_-physician) of 77%, respectively. VQ technique significantly reduced the mean processing time from 18.6 seconds to 2.16 seconds for one image.
**Conclusion:** Our preliminary study demonstrated great potential of CAD in assisting endoscopists to detect abnormal microvessels of EGC in M-NBI images.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0676 NOVEL ENDOSCOPIC FINDINGS OF MULTIPLE WHITE FLAT LESIONS: A NEW SUBTYPE OF HYPERPLASTIC POLYPS IN THE STOMACH

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**Introduction:** Benign, non-neoplastic gastric polyps consist of hyperplastic polyps of foveolar epithelium type and fundic gland polyps. However, recently we have detected a different type of polyp, in the form of multiple white flat lesions (MWFL),which are present from the gastric body to the fundus. There is no report in the literature describing endoscopic findings and clinical significance of these lesions.
**Aims & Methods:** We retrospectively studied the endoscopic findings—including findings by magnification endoscopy with narrow-band imaging (NBI)—and the clinical characteristics of patients with MWFL. The study population consisted of consecutive patients who underwent upper magnifying gastrointestinal endoscopy (GIF-Q240Z, Olympus Co., Ltd., Tokyo) between April 2014 and March 2015 at a single center.by an endoscopist with more than 15 years' experience in performing magnifying endoscopic examinations in the stomach Patients who had undergone total gastrectomy and patients for whom detailed medical notes were not available were excluded from the study. Three types of images (conventional endoscopic images, NBI non-magnified images, and NBI magnified images) recorded onto an endoscopic filing system were reviewed and the endoscopic findings characteristic for MWFLwere investigated. The patients' background clinical information recorded in medical notes was also reviewed, and the clinical data of patients was compared according to whether or not they exhibited MWFL. Chi-square test was used for statistical analysis and statistical significance was set at $p < 0.05$.
**Results:** A total of 177 consecutive patients were included in the analysis. The prevalence of MWFL was 7.3% (13/177 patients). Endoscopic findings characteristic for MWFL were as follows. Conventional white-light endoscopy findings revealed small, white superficial elevated multiple lesions of various sizes with serrated margins in all MWFL patients. By non-magnifying endoscopy with NBI, the background mucosa appeared brown, thus enhancing the contrast with the white lesions and making them easier to identify. By magnifying endoscopy with NBI, a clear demarcation line was present between the lesion and the background mucosa. The microvasculature of the lesions was not clearly visualized. Individual marginal crypt epithelium had an elongated, elliptical appearance with a uniform shape. Comparison between MVFL-positive and -negative patients revealed that the MVFL were frequently present among the elderly ($p = 0.007$) patients and women ($p = 0.089$). Furthermore, The prevalence of MVFL-positive patients who were taking oral antacid medication (100%, 13/13) was higher than that of MVFL-negative patients (53.7%, 88/164) ($p < 0.001$).
**Conclusion:** Endoscopic findings of MWFL are totally different from those of hyperplastic polyps of foveolar epithelium type and fundic gland polyps. The presence of MWFL might be related to the use of antacids such as proton pump inhibitors (PPI). MWFL, therefore, could constitute a new disease entity that endoscopists need to be aware of.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0677 IMPACT OF TIME TO ENDOSCOPY ON MORTALITY IN PATIENTS WITH NON VARICEAL UPPER GI BLEED

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**Introduction:** Acute upper GI Bleed (AUGIB) is one of the most common presentations in UK hospitals and is associated with significant morbidity and mortality. Current guidelines recommend early endoscopic intervention (i.e. Within 24 hours) for patients presenting with UGIB.1 Early endoscopy can be beneficial in achieving hemostasis more quickly & decreasing need for transfusions. 2. However aggressive resuscitation before rushing towards an endoscopy has its own importance as inadequate early resuscitation is believed to be a major factor in the persistently high mortality rate in patients with UGIB.3
**Aims & Methods:** We conducted a retrospective study of 696 patients who were admitted to Cardiff and Vale university health board & subsequently treated in endoscopy unit for non variceal upper GI bleed between September 2010 and September 2013. Patients were divided into 3 groups depending upon the time to scope from admission (Within 6 hours, 6–24 hours and more than 24 hours).
**Results:** Our study found that very early endoscopy (i.e. <6 hours) compared to rapid endoscopy (6–24 hours), did not improve outcome and in fact had a significantly worse mortality rate of 16.67% vs 4.62%. Though it can be argued that patients who had a very early endoscopy were more unwell comparatively. When we compared patients in high risk group only i.e. GBS (Glasgow Blatchford >10); results were identical.

Time to scope vs Outcome

| Hours to OGD | Total Number | Death |
|---|---|---|
| <6 hours | 18 | 3(16.67%) |
| 6–24 Hours | 173 | 8(4.62%) |
| >24hours | 505 | 59(11.68%) |

**Conclusion:** Our study reinforced the importance of access to rapid endoscopic intervention within 24 hours, but did not demonstrate the need for very early gastroscopy. This was likely due to the fact that organizing very early endoscopy within 6 h would slow intensive resuscitative efforts leading to worse outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0678 APPLICATION OF A NOVEL ENDOSCOPIC SUTURING COIL IN ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)

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**Introduction:** Endoscopic submucosal dissection (ESD) is a relatively new but widely used medical technique that has been used to remove gastrointestinal mucosal tumors.
**Aims & Methods:** To evaluate a new suture coil technique for endoscopic submucosal dissection (ESD). We performed a retrospective analysis of the treatment and outcomes of 15 patients who underwent ESD for early gastrointestinal cancer between December 2013 and September 2014. The new coil-assisted suturing technique aided in lifting the mucosa, thereby fully revealing the submucosal layer and facilitating submucosal dissection. The suture coil was also used to close postoperative wounds.
**Results:** This new suture coil technique successfully aided in the resection of lesions from all 15 patients. Specifically, the use of the coils to retract the mucosa allowed the submucosal blood vessels to be clearly visualized, intraoperative uncontrollable bleeding did not occur, and the coil-based portion of the procedure was completed in 5–10 min. However, in one patient a small perforation did occur with the use of this new technique, and the perforation was readily stitched using the novel suture coil technique. In two other patients, titanium clips that had the suturing coils attached slipped after being applied, and this required adjustment of the ESD approach. The suturing coils were also found to be effective for wound closing in all of the patients. While one patient did experience minor postoperative bleeding, it was controlled with a hemostatic clip that was applied during a second endoscopy.
**Conclusion:** The proposed novel suture coil technique is straightforward to use, facilitates ESD, and it has the potential to reduce the likelihood of intraoperative and postoperative ESD-related complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0679 EFFICACY OF MAGNIFYING ENDOSCOPY WITH BLUE LASER IMAGING FOR DIAGNOSIS OF RANGE OF EARLY GASTRIC CANCER

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**Introduction:** Diagnosis of range of early gastric cancer (EGC) is essential for ESD, which is a standard treatment for EGC. Recently, it is reported that image-enhanced endoscopy with magnifying endoscopy (IEE-ME) is useful for diagnosis of range of EGC. However, IEE-ME is not considered gold standard for diagnosis of range of EGC yet. We prospectively evaluated whether magnifying endoscopy with blue laser imaging (M-BLI) could be a gold standard for diagnosis of range of EGC.
**Aims & Methods:** 47 patients with 50 tumorous lesions including 34 well-differentiated EGCs and 16 gastric adenomas were enrolled in this study between July 2015 and February 2016. Excluding lesions were diagnosed moderately and poorly differentiated EGC by biopsy specimen before M-BLI. After 50 lesions were detected a clear demarcation line using M-BLI, all of 50 lesions were randomly divided into two groups, which were only M-BLI observation

group (A group N = 25) and M-BLI with additional negative biopsies group (B group N = 25). All of the lesions were resected by ESD. Primary end point was to evaluate diagnostic accuracy of M-BLI and rate of complete resection between two groups. Secondary end point was to evaluate clinicopathological features such as mean age, gender, location, macroscopic type, median tumor size, and finally pathological diagnosis were compared between two groups.
**Results:** Diagnostic accuracy of M-BLI in A group and B group were 100% and 98%, respectively. Rate of complete resection in A group and B group were 100% and 100%, respectively. There was no significantly difference for diagnostic accuracy and complete resection rate between two groups. No significant difference was found in the clinicopathological features between A group and B group as follows; mean age was 72.8 and 72.8, gender (male:female) was 16:9 and 15:10, macroscopic type (slightly elevated: flat: slightly depressed) was 9:1:15 and 13:1:11, median tumor size was 13.1 mm and 15.7 mm, finally pathological diagnosis (adenoma: well differentiated adenocarcinoma: papillary adenocarcinoma: moderately differentiated adenocarcinoma) was 2:20:1:2 and 0:23:0:2, and location (U:M:L) was 0:10:5 and 6:10:9, respectively.
**Conclusion:** M-BLI is an effective tool for diagnosis of the range of EGC. When M-BLI showed clear demarcation lines, there were no need of additional negative biopsy around EGC. Our study suggested that M-BLI can be a gold standard for diagnosis of the range of well differentiated gastric adenocarcinoma.
**Disclosure of Interest:** Y. Itoh: Y. Itoh was affiliated with a department that was partially funded by Fujifilm Medical Co., Ltd. (J082003006).
All other authors have declared no conflicts of interest.

## P0680 THE IMPACT OF THE UNITED KINGDOM NATIONAL OESOPHAGO-GASTRIC CANCER AWARENESS CAMPAIGN

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**Introduction:** The national oesophago-gastric cancer campaign was launched in late January 2015 for 4 weeks with the intention to raise awareness and increase detection of upper GI cancers.
**Aims & Methods:** The aim of our study was to evaluate the impact of this campaign on the number of 2 week wait (2WW) referrals for gastroscopies, diagnosis of new upper GI cancers and other major pathologies identified during diagnosis. A retrospective audit was undertaken on all patients who were referred through the 2WW pathway for gastroscopy for the month before, during and after the campaign at a district general hospital trust. Data on indication, patient demographic and endoscopic diagnosis was noted. Major pathology was defined as that requiring biopsy and/or repeat procedure.
**Results:** A total of 739 patients were assessed during the study period, with a mean age of 64 years (SD 14.7) and 43% male. The indication for gastroscopy was dyspepsia in 43.3%, dysphagia in 34.9%, both dyspepsia and dysphagia in 5.0% and other indications in 16.6%. There was a 70% increase in the number of 2WW referrals during the campaign over the preceding month, with a sustained increase of 50% the month after. Despite the increase in referrals the incidence and total number of cancer detected, fell from 7.4% (n = 13) before the campaign month, to 2.3% (n = 7) during and 3.4% (n = 9) after (p = 0.02). Findings of major pathology did not significantly change either; 17.0% (n = 30) before, 17.7% (n = 53) during and 15.2% (n = 40) post (p = 0.71). There was no alteration on the tumour stage of cancers detected during or after the campaign. However, the proportion of cancers diagnosed in the <55years of age group increased from 7.7% (n = 1) before to 28.6% (n = 2) during and 11.2% (n = 1) post campaign (p = 0.54).
**Conclusion:** The 'Be clear on cancer' oesophago-gastric campaign significantly increased the number of 2WW referrals for gastroscopies without any increase in detection of new cancers or major pathologies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0681 SAFETY AND USEFULNESS IN ELDERLY PATIENTS 80 YEARS OR OLDER OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC AND ESOPHAGEAL CANCERS

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**Introduction:** Endoscopic submucosal dissection (ESD) is a safe and effective treatment modality for early gastrointestinal neoplasms. Given the increasing life expectancy worldwide, there is growing number of elderly patients referred for endoscopic treatment of early gastrointestinal cancer. ESD can be performed in the endoscopy room under sedation administered by endoscopists, however there are currently no guidelines on the best anesthetic modality, particularly in elderly patients, who are at higher risk of complications given frequent concomitant comorbidities, The aim of this study was to assess the safety and effectiveness in elderly patients of ESD for early gastric cancer (EGC) or early esophageal cancer (EEC).
**Aims & Methods:** We retrospectively investigated 2015 consecutive patients with 2276 lesions who underwent ESD for EGC/EEC between January 2011 and December 2015 at our institution. Anesthetic modalities included: i. propofol-based monitored anesthesia care (MAC) administered by the anesthesiologist without intubation; ii. regular sedation by endoscopists with pentazocine hydrochloride plus midazolam or/and propofol; iii. general anesthesia (GA) in the operating theatre. Anesthetic modality was at discretion of the endoscopist and anesthesiologist based on the technical complexity of the case and patient comorbidities [1]. In this study, patients were divided into 2 groups based on age 80 years or older (Group A, n = 255) and less than 80 years (group B, n = 1760). Patient demographics, sedation methods, technical outcomes, adverse events, body movement that required control by a third person during ESD, oxygen saturation (SpO2), sedatives and dosages given were then examined.
**Results:** The group A/B included 183/1367 males and 72/393 females with a mean age of 83.1/67.8 years. In the group A/B, 246/1610 ESDs for 252/1644 EGCs and 35/343 ESDs for 35/345 EECs were performed, in which 204 (80%)/1439 (81.8%) patients were managed by regular sedation by endoscopists, 46 (18%)/311 (17.7%) patients by propofol-based MAC without intubation, and 5 (2%)/10 (0.6%) patients by GA. The median size of EGC and EEC in the group A/B were 15 mm (range, 2.5–89)/12 mm (1–74) (P < 0.001) and 25 mm (7–60)/20 mm (3–100) (P < 0.001), respectively. The proportions of class III in the ASA classification in the group A/B were 1.9% (I-II/III, 250/5)/0.4% (I-II/III; 1752/8), respectively (p < 0.001). Technical outcomes and adverse events for the groups A/B were as follows: median procedure times were 74/76 minutes (range, 10–442/16–425) (p = 0.5); rate of en-bloc resection was 99.6%/99.5% (p = 0.72); perforations occurred in 0.7%/1.3% of patients (p = 0.53) and delayed bleeding in 7.1%/3.8% (p = 0.16). No significant differences in body movement of 47%/43% (p = 0.97), and median SpO2 of 98% (72–100)/98% (57–100) (p = 0.84) were seen in the two groups. Sedation was controlled by using propofol in 183/1334 (74%/83%) ESDs for EGCs and in 35/343 (100%/100%) ESDs for EECs and the remaining were managed by midazolam. Median dose of propofol in the group A/B were 5.6 mg/kg/h (range, 1.2–11.2)/6.7 mg/kg/h (0.5–25.0) (p < 0.0001) while median dose of midazolam in the group A/B were 0.12 mg/kg/h (0.01–0.29)/0.12 mg/kg/h (0.01–0.60) (p = 0.47). Five ESD were discontinued because of laryngeal edema due to the overtube (n = 2), severe esophageal spasm (n = 1) and cardiovascular instability (n = 2).
**Conclusion:** ESD is a safe and effective treatment modality for early EGC and EEC in patients 80 years or older with no differences in the short-term outcomes compared to younger patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0682 COMPARISON OF LANSOPRAZOLE WITH VONOPRAZAN FOR TREATING POST-ENDOSCOPIC SUBMUCOSAL DISSECTION ULCERS

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**Introduction:** Post-endoscopic submucosal dissection (ESD) ulcers are treated with proton pump inhibitors (PPIs). This is because some meta-analyses found that peptic ulcers are curable earlier with PPIs than with H2 receptor antagonists (H2RA) owing to the stronger inhibitory effect of PPIs on gastric acid secretion. Vonoprazan (VPZ) has been available since February 2015 in Japan. VPZ is a potassium-competitive acid blocker, which is a new gastric acid suppressant. VPZ has a more potent and long-lasting anti-secretory effect than conventional PPIs. There is no report examining whether VPZ is superior to PPIs in healing post-ESD ulcers or preventing post-ESD bleeding. We compared the rate of decrease in ulcer size in patients with post-ESD ulcers treated with PPI or VPZ.
**Aims & Methods:** We conducted ESD in 37 patients with gastric tumors, from April 2015 to March 2016. Subjects were randomly divided into the lansoprazole (LPZ) group or VPZ group. Both groups received an anti-ulcer drug orally for 8 weeks; the LPZ group received lansoprazole 30 mg/day and the VPZ group received VPZ 20 mg/day. Patients in both groups underwent upper gastrointestinal endoscopy at 4 and 8 weeks after the start of treatment. The ESD-induced ulcer size was assessed by area ($mm^2$); long and short axes (mm) of an assumed ellipse were measured using an endoscope and measuring equipment to calculate ulcer size (long radius×short radius×$\pi$= ulcer size). Complete healing was defined as ESD ulcer reaching the scar stage (S1 or S2 stage).
**Results:** The LPZ group consisted of 14 men and 3 women with a mean age of 75.6 years, whereas the VPZ group consisted of 12 men and 6 women with a mean age 71.7 years. In the LPZ group, the 17 lesions consisted of 4 in the body, 3 in the angulus, and 10 in the antrum. In the VPZ group, the 18 lesions consisted of 2 in the body, 8 in the angulus, and 8 in the antrum. There were no significant differences in extraneous factors (body mass index, degree of atrophic gastritis, and *Helicobacter pylori* infection status) between the two groups. Mean (SD) ulcer size at baseline was 2927.5 (1978.4) $mm^2$ in the PPI group and 3286.7 (2550.1) $mm^2$ in the VPZ group, and were not significantly different from each other (p = 0.64). Mean (SD) ulcer sizes at 4 and 8 weeks after ESD were 175.8 (289.3) $mm^2$ and 11.2 (9.4) $mm^2$ in the PPI group, and 360.0 (525.2) $mm^2$ and 35.2 (98.3) $mm^2$ in the VPZ group respectively. There were no significant differences between the two groups (p = 0.21 at 4 weeks and p = 0.37 at 8 weeks). The

rates of decrease in ulcer size were 93.5% for LPZ group and 88.6% for VPZ group, at week 4; and 99.2% for LPZ group and 99.6% for VPZ group, at week 8. There were no significant differences between the two groups at week 4 ($p = 0.12$) and week 8 ($p = 0.44$). No patient had complete healing at week 4 in both groups. The rate of complete healing at week 8 was 87.5% for LPZ group and 57.9% for VPZ group, and no statistically significant difference was found between the two groups ($p = 0.053$). There was one patient with post-ESD bleeding in each group.
**Conclusion:** VPZ did not reveal any superiority in healing post-ESD ulcer compared with LPZ; therefore, PPIs might be sufficient for post-ESD ulcer treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0683 OVER-THE-SCOPE CLIP FOR THE MANAGEMENT OF ENTEROCUTANEOUS FISTULA (ECF) AND PERISTOMAL LEAKAGE

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**Introduction:** Persistent enterocutaneous fistula (ECF) following enteral tube removal occurs in 10% of patients. Persistent leakage results in cutaneous infection, irritation and dehydration. Several factors can delay the closure of the tract and contribute to persist ECF. Prolonged tube placement for more than six months duration result in epithelialization of the tract which plays a critical role in development of persistent ECF. Hence de-epithelialization may be important in treatment. The over-the-scope clip (OTSC) has been demonstrated to be effective for leaks and perforations with efficacy for fistulae closure being less well established. OTSC is a new class of clipping system that has the ability to precise and easy clouser for large defect upto 30 mm in diamter. There are several case reports and case series of its use in gastrocutaneous fistula but efficacy in large series has not been documented.
**Aims:** To assess the technical success, clinical success, and adverse events when using the OTSC for persistent ECF.
**Methods:** We report a single-center retrospective review of patients with persistent ECF following gastrostomy or jejunostomy tube removal who underwent OTSC closure. Persistent ECF was defined as persistent leakage for more than 1 week after removing the feeding tube. Technical success was defined as satisfactory application of the OTSC resulting in immediate fistula closure. Clinical success was defined as resolution of leakage after placement of the OTSC at last available follow-up.
**Results:** A total 16 patients (mean age 54, 69% Female) were included in the analysis. Fourteen patients had PEG tube and two had jejunostomy tube placement with a median time of percutaneous tube dwell of 22 months (range 1–48). The median duration of persistent ECF was 21 days (range 8–60). The median size of the fistula was 10 mm (range 5–15). ECF was ablated with argon plasma coagulation (APC) prior to OTSC placement in 87.5% of patients. Technical success was achieved in all patients (100%). The median follow up post OTSC placement was 30 days (range 3–120). Overall clinical success was accomplished in 62.5% of cases (10/16 patients) without any adverse events. Two patients who failed OTSC were managed successfully with alternative endoscopic therapies, 3 were managed surgically and 1 died of unrelated causes.
**Conclusion:** Endoscopic closure of ECF using the OTSC with endoscopic ablation of the fistula tract is a moderately effective and safe. About a third of patients fail therapy and can be managed by alternative endoscopic or surgical modalities.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0684 EXPANDING RELATIVE INDICATION OF ESD FOR EARLY GASTRIC CANCER ACCORDING TO THE SURGICAL CASES OF POST NON-CURATIVE ESD

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**Introduction:** Recently endoscopic submucosal dissection(ESD) for early gastric cancer (EGC) has been gaining popularity. Expanded indication criteria is also accepted at this time in addition to the absolute indication criteria. Criteria of ESD had been decided based on the R0 resection and a very low risk of lymph node (LN) metastasis. On the other hands, the lesion had about 10% risk of the LN metastasis, for example submucosal (SM) invasion over 500 μm, is expected to resect at the 90% probability. With the advance in aged society, ESD is one of the choices of the treatment for the EGC to the patients who are not able to have surgery because of chronic diseases.
**Aims & Methods:** This is the study of 62 patients who underwent gastrectomy after ESD for EGC because the lesion was pathologically over the indication of ESD between March 2007 and February 2016 at our hospital. 17 patients had LN metastasis and/or residual tumor (R1 group), and 45 patients had no LN metastasis and residual tumor (R0 group). We retrospectively analyzed the pathological features between two groups.
**Results:** Regarding the characteristics of patients, in age, gender, location of the lesion, tumor size, there were no significant differences between two groups. In gross type, protruded lesion in R1 group was significantly more frequent than R0 group ($p = 0.04$). Then, we analyzed the character of the lesion according to the depth of invasion and the invasion of the lymphatic vessels. In differentiated adenocarcinoma, 1) 2 of 7 patients that had 500 μm or less SM invasion and over 30 mm in size (2/7:29%), 2) 7 of 37 patients that had over 500 μm SM invasion (7/37:19%), 3) 7 of 31 patients that had invasion of lymphatic vessels (7/31:23%), 4) 7 of 11 patients that had invasion both of SM and lymphatic vessels (7/11:24%), and 5) all 2 patients that had invasion SM and lymphatic vessels with ulcer change (2/2:100%), had LN metastasis. In undifferentiated adenocarcinoma, 2 patients that the lesion of protruded type (Type I) had residual tumor in muscle layer of resected tissue (2/2:100%). 16 patients had differentiated carcinoma including undifferentiated carcinoma, and 12 of them had LN metastasis (12/16:75%). Only 1 of 10 patient with differentiated type without papillary type, SM2 invasion, no lymphatic vessels invasion and resection margin negative had LN metastasis (1/10:10%).
**Conclusion:** With the advancement of endoscopic devices, we have widen the limitation of ESD. In case that the lesion is over the ESD indication, it is better that we recommend the patient to have the gastrectomy because of the high rate of LN metastasis. However, in case the patient have a severe complications, we should think about necessity of the additional gastrectomy based on pathological findings of ESD tissue.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0685 THE EFFECTIVENESS OF THE TRIAMCINOLONE-LOADED THERMOGEL SYSTEM TO PREVENT ESOPHAGEAL STRICTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION IN A PORCINE MODEL

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**Introduction:** Esophageal stricture, as an important complication of endoscopic submucosal dissection (ESD) in the esophagus, can cause dysphagia, reduce the quality of life significantly. Repeated endoscopic balloon dilation (EBD) was performed before stricture formation to prevent esophageal stricture previously, but repeated EBD increases trauma and cost of the treatment. Then triamcinolone was gradually used in prevention for esophageal stricture after ESD, and was confirmed to be able to prevent stricture occurrence. But there are still advantages of triamcinolone for submucosal injection, for example, it has short duration of drug function, drug function intensity can not continue to cicatrization fastigium, repeated rejection brings patients much inconvenience and pain. The thermogelling PLGA-PEG-PLGA triblock copolymer was verified to be a good drug controlled release carrier.

**Aims & Methods:** The study aimed to discuss the effectiveness of triamcinolone-loaded thermogel system to prevent esophageal stricture after ESD. ESD was performed in middle esophagus in six porcine models, the resected mucosa occupied complete circumference, the longitudinal diameter was 4–5 cm. Gastroscopy was performed on the 1st, 2nd, and 4th week after ESD, the situation of esophageal stricture was observed, porcine models of esophageal stricture after ESD were set up. According to different reagents injecting into the wound after ESD, eighteen porcine models were divided into 3 groups, blank control group (n = 6), triamcinolone injecting group (n = 6) and triamcinolone-loaded thermogel system injecting group (n = 6). Blank thermogel solution was injected in blank control group. The volume of injecting regent in each group is 25 ml. The total dose of triamcinolone was 100 mg in each of the latter two groups. Gastroscopy was performed on the 2nd, 4th, and 8th week after ESD, the situation of esophageal stricture after ESD in the three groups was observed and compared.
**Results:**

**Table 1:** Comparison of severe esophageal stricture between triamcinolone-loaded thermogel system injecting group and blank control group

| | Triamcinolone-loaded thermogel system injecting groupn = 6 | Blank control groupn = 6 | P-value Two-tailed |
|---|---|---|---|
| No or mild esophageal stricture (lumen diameter) 1.0 cm | 3 | 0 | 0.01P0.05 |
| Moderate esophageal stricture lumen diameter 0.5–1.0 cm | 2 | 0 | |
| Severe esophageal stricture lumen diameter 0.5 cm | 1 | 6 | |

On the 4th week after ESD in middle esophagus, the esophageal stricture rate in the six porcine models was 100%, porcine models of esophageal stricture after ESD were set up successfully. According to the gastroscopy result after ESD in the three groups, the rate of moderate and severe esophageal stricture (lumen diameter≤1.0 cm) in blank control group, triamcinolone injecting group and triamcinolone-loaded thermogel system injecting group was 100% (6/6), 83.3% (5/6) and 50% (3/6), respectively. Compared with blank control group, both of triamcinolone injection and triamcinolone-loaded thermogel system injection could not prevent postoperative esophageal stricture completely (P > 0.05, respectively). Compared in esophageal stricture extent, the rate of severe esophageal stricture (lumen diameter < 0.5 cm) in blank control group, triamcinolone injecting group and triamcinolone-loaded thermogel system injecting group was 100% (6/6), 66.67% (4/6) and 16.67% (1/6), respectively. Compared with blank control group, triamcinolone injection could not decrease the degree of postoperative esophageal effectively (P > 0.05), while triamcinolone-loaded thermogel system injection could decrease the degree of postoperative esophageal stricture, the difference was statically significant (0.01 < P < 0.05) (Table 1).
**Conclusion:** Compared with blank control group, both of triamcinolone injection and triamcinolone-loaded thermogel system injection could not prevent postoperative esophageal stricture completely, however, triamcinolone-loaded thermogel system injection could decrease the degree of postoperative esophageal stricture, while triamcinolone injection could not decrease the degree of postoperative esophageal stricture effectively.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0686 THE ROLE OF MINIPROBE ENDOSCOPIC ULTRASONOGRAPHY IN THE DECISION OF EARLY GASTRIC CANCER TREATMENT

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**Introduction:** The exact prediction of tumor invasion depth is mandatory to perform endoscopic submucosal dissection (ESD).
**Aims & Methods:** The aim of this study is to evaluate the accuracy of endoscopic ultrasonography (EUS) predicting invasion depth accordingto the degree of authenticity for endoscopic depth prediction and to find the characteristics of lesions associated with abenefit of additional EUS after endoscopy. Between January 2009 and February 2015, 275 well to moderate differentiated early gastric cancer (EGC) in 269 patients underwent EUS and curative treatment. We reviewed their medical records including preoperativeconventional endoscopy (CE) and EUS staging.
**Results:** The accuracy of CE and EUS to identify lesions meeting expanded ESD indications was 90.4% and 91.4% (p = 0.727) for lesion with high degree of certainty, 50.6% and 68.8%, respectively, for low degree of certainty (p = 0.021). Lowdegree of certainty for endoscopic depth prediction (OR 3.168; CI 1.256–7.990), lesions with submucosal invasion on CE staging (OR 3.7, CI 1.3–10.7), ulcer including scar (OR 5.3; CI 1.5–18.5) were associated with a higher accuracy of EUS than CE for identifying lesion meeting expanded ESD indications.
**Conclusion:** In lesions with indefinite endoscopic T staging, submucosal invasion on CE staging and ulcer including scar, EUS staging could be helpful in the decision-making process for treatment of patients with EGCs according to expanded indications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0687 USEFULNESS OF THE MARGIN AROUND LESION FINDINGS BY MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING IN EARLY GASTRIC CARCINOMA

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**Introduction:** Many endoscopists have reported their own classifications of early gastric carcinoma using magnifying narrow-band imaging. However, there are few reports on the classification of the margin around lesions by magnifying narrow-band imaging. The aim of this study was to advocate the usefulness of the "demarcation area classification" for the diagnosis of early gastric carcinoma.
**Aims & Methods:** 197 lesions that could be investigated by magnifying narrow-band imaging were included in this study. They consisted of 115 early gastric carcinoma and 82 intestinal metaplasia. We suppose that white zone changes (fusion sign and erasure sign) and blood vessel changes (extend sign and draw sign) are indications of early gastric carcinoma findings; we retrospectively investigate this hypothesis to see if it is valid.
**Results:** For the investigation of white zone in demarcation area, both fusion sign (P: < 0.0001) and erasure sign (P: < 0.0001) were observed more often in early gastric carcinoma rather than in intestinal metaplasia. When we diagnosed the lesion with either a fusion sign or erasure sign as early gastric carcinoma, accuracy was 80.7%. For the investigation of blood vessel in demarcation area, both extend sign (P: < 0.001) and draw sign (P: < 0.0001) were observed more often in early gastric carcinoma rather than intestinal metaplasia. When we diagnosed the lesion as early gastric carcinoma with either extend sign or draw sign, accuracy was 59.9%.
**Conclusion:** The estimations of white zone and blood vessel in demarcation area are useful for diagnosis of early gastric carcinoma.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0688 THE TUNNEL + CLIP STRATEGY INCREASES THE EASE AND SPEED OF OESOPHAGEAL ESD: A RANDOMIZED STUDY IN PIGS

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**Background and Aims:** Oesophagus is considered as one of the most difficult location in which to perform ESD. Indeed its narrow diameter compromises scope manoeuvrability and the thin wall increases the risk of perforation. However, oesophageal ESD is often essential, as indicated by the epidemiology of early-stage oesophageal cancer in Europe, and the high morbidity associated with oesophageal surgical procedures. Counter-traction methods and tunnel ESD have been previously reported to help during oesophageal ESD. We first reported the combination of the clip-with-line method and the tunnel technique (tunnel + clip strategy) to facilitate oesophageal ESD[1].
**Patients and methods:** From July 2015 to April 2016 we performed a randomized study in pigs comparing oesophageal ESD using the Tunnel + clip strategy vs oesophageal ESD using the tunnel method. After creating a virtual lesion in the oesophagus of 35 kgs anesthetized Landrace mini-pigs with a polypectomy snare using a soft coagulation current, a tunnel was created beneath this lesion after distal and proximal mucosal incision. Then a randomization was performed to finish the procedure with or without adding a clip with line in traction dropped at the proximal entry of the tunnel. Pig R0 resection, monobloc resection, speed of the dissection, perforation were compared. An evaluation of operator comfort and perception of safety (dissection score) was performed using a visual analogue scale (0 = the worst, 10 = the best). We estimated that a sample of 16 resections would provide at least 90% power and an alpha level of 5% to prove an increase of the speed of 50%.
**Results:** Twenty virtual lesions were resected: 10 with the tunnel method and 10 using the tunnel + clip strategy. The speed of dissection was 1.8 faster in tunnel + clip group: 15 $mm^2$/min vs 8.3 $mm^2$/min (p = 0.002). No perforation occurred in each group. The dissection score was significantly higher in the Tunnel + clip group than in the Tunnel group (7.3 vs. 4.7; p = 0.006) indicating that both operators felt more comfortable and safer performing oesophageal ESD using the tunnel + clip strategy. No difference was observed in the rates macroscopic R0 resection (100% vs 70% p = 0.2) and of en bloc resection (100% vs 90%, p = 1) The clip provided considerable assistance in performing the procedure. No macroscopic damage caused by the clipping was reported.
**Conclusion:** The tunnel + clip strategy for oesophageal ESD increases the ease and the speed of oesophageal ESD in pigs compared to the classic tunnel method. The tunnel + clip strategy improves the field of view during oesophageal dissection in particular for the edges of the tunnel. This technique enabled standardisation of the ESD procedure for superficial oesophageal neoplasia. This strategy allows a constant good exposure of the submucosal layer that is key for efficient and safe ESD. This strategy could become the standard for endoscopic resection of superficial oesophageal cancerous lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0689 ENDOSCOPIC RESECTION FOR DUODENAL LESIONS: OUTCOMES OF THE 374 PATIENTS FROM A RETROSPECTIVE SINGLE-CENTER STUDY

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**Introduction:** Endoscopy resection (ER), a minimally invasive technique, is becoming increasingly utilized to treat duodenal lesions. Several reports have been published, but mostly involved only a small number of patients.

**Aims & Methods:** The aim of this study was to assess the feasibility, efficacy, and safety of ER for duodenal lesions in a large retrospective study. We retrospectively analyzed the medical records of a total 374 patients with duodenal lesions who underwent ER at our institution from January 2008 to February 2015.

**Results:** The mean lesion size was $12.5 \pm 9.0$ mm. ER was in the form of 51 polypectomys (13.6%), 147 endoscopic mucosal resection (39.3%), and 176 endoscopic submucosal dissection (47.1%). The mean procedure time was $19.8 \pm 14.1$ minutes. The total rates of en bloc resection and complete resection were 94.7% and 89.0%, respectively. Intraoperative bleeding was observed in 1 patient whereas delayed bleeding was observed in 12 patients. 1 patient had intraoperative perforation while 3 patients had delayed perforation. The results of multivariate analyses showed that histopathology ($p = 0.004$) was significantly influencing delayed bleeding; histopathology ($p = 0.000$) and lesion size ($p = 0.027$) for en bloc; and histopathology ($p = 0.000$), lesion size ($p = 0.000$) and treatment methods ($p = 0.004$) for complete resection. During a mean follow-up period of $22.2 \pm 17.8$ months, 2.9% recurrence rate for dysplastic lesion (2/68) was recorded. One patient died from metastases of a primary duodenal adenocarcinoma after additional surgery, resulting in a disease-specific survival rate for dysplastic lesion was 98.5%.

**Conclusion:** ER can be considered as an effective, feasible and minimally invasive method for duodenal lesions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0690 IMPROVING EFFICIENCY IN THE ENDOSCOPY UNIT: WHAT CAN WE DO TO REDUCE 'DID NOT ATTEND' (DNA) AND LATE CANCELLATION RATES?

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**Introduction:** The demand for gastrointestinal endoscopy is inexorably growing in the UK because of the expanding screening programme for colon cancer, the two week waiting time for suspected GI cancer and the expectation from the NHS Operating Framework that 99% of patients should have their diagnostic tests within 6 weeks. In our endoscopy unit, demand for endoscopy is outstripping capacity and this gap is growing. It is therefore more relevant and important than ever before to improve the efficiency of the unit – the easy targets being increasing the room occupancy rate and decreasing the DNA rate which seems to be increasing.

**Aims & Methods:** To audit the efficiency in the endoscopy unit focusing on room occupancy, DNA and late cancellation rates with a view to implementing changes to improve efficiency. Also to look for patterns in list utility in relation to the day of the week and timing of the list. The standard endoscopy list contains 11 points (gastroscopy/sigmoidoscopy 1 point, colonoscopy 2 points) with evening, screening and teaching lists reduced to 8 points. We interrogated the electronic databases to obtain a number of variables on all endoscopy lists between April 2015 and August 2015 (19 weeks).

**Results:** During the study period a total of 3752 patients (5788 points) were listed for endoscopy. 546/584 lists ran as planned (room occupancy 93.5%) with 38 either cancelled or converted to other procedures. There were 504 (92.3%) weekday lists and 42 (7.7%) weekend lists. The average number of lists run on a working week day was 5.4. Overall 11.9% ($n = 446$) patients did not attend without prior notice and 7.7% ($n = 288$) patients cancelled without sufficient time to rebook the appointment. In total, 19.6% of patient appointments were not undertaken. 35.1% ($n = 195$) of lists ran at full capacity without any patients in the DNA or late cancellation categories. DNA and late cancellation rates did not vary much between week days but were considerably lower for weekday morning (14.7%) and weekend morning (10.1%) appointments compared to afternoon (22.2%) and evening (21.1%) lists. There were 93 acute lists run. These consist of some elective patients and empty spaces for emergency patients. 72.2% of elective acute list capacity was booked and undertaken. All booked elective patients on acute lists were scoped.

**Conclusion:** Our study showed an overall efficiency of 80.4% and a room occupancy of 93.5%. This amounts to a significant loss of earnings over the given period and leaves considerable room for improvement. Patients are more likely to attend weekend and AM appointments versus PM or evening appointments. Further study in to the contributing factors is advised as results may yield which can be used to increase efficiency of PM and evening slots. Based on these results a number of measures have been implemented to try and increase efficiency of the endoscopy unit. The following solutions are currently being explored: patient education, overbooking lists by 10%, weekly analysis of future lists to ensure cancellations are replaced, phoning patients five days before their appointments (increased administrative costs) and warehousing a number of pre-assessed patients who can attend at short notice. The authors note that, as has been mentioned in General Practice, it may be that taking a fee from patients, refundable on attendance to endoscopy appointment, is a good solution. However this is not currently viable at this time.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0691 PERCUTANEOUS ENDOSCOPIC JEJUNOSTOMY AS THERAPEUTIC INDICATION IN PATIENTS WITH PARKINSON'S DISEASE

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**Introduction:** PEJ is miniinvasive endoscopic procedure for nutritional or therapeutic indication. It is more difficult as PEG from technical point of view. PEJ was used in patients with Parkinson's disease for application of antiparkinsonic medication.

**Aim:** Evaluation of PEJ in patients with Parkinson's disease from therapeutic indication. Jejunal administration of medication (carbidopa and levodopa) was the aim with the continual application of medicine to jejunum and achievement of stable blood levels.

**Patients and Methods:** At the endoscopic ambulance of the 3rd Department of Medicine od Medical University 31 PEJ were done in patients with Parkinson's disease in the period from 1. 1. 2009 till 10. 10. 2015. The indication was the late stage of Parkinson's disease, if deep brain stimulation was contraindicated or non-agreement in levodopa-responsive patients. Hypersensitivity to levodopa/carbidopa, glaucoma, severe kidney, liver or cardiac failure, acute stroke, feochromocytoma, hypertyreosis and con-compliance were contraindication of the procedure.

**Results:** Fruitfulness of implantation PEJ was 100% and medium persistence was 818 days. We achieved higher persistence of PEJ in comparison with the literature (1–2 years). From the gender point of view men: women were: 1:1.2. Medium age was 70 years. Complication in association with the procedure were present in 57.1%, mild in 53.6% severe in 3.6%, comparable with the literature. Obturation of the probe was the most common complication (33.3%), comparable with the literature. It was associated with the small diameter of our probes (9 Fr). The second most common complication was (non)-intended removal of the probe (18.75%), present more frequent as in the literature. The cause was indication diagnosis – advanced stage of Parkinson's disease with demention and limited patient cooperation. Jejunal Levodopa administration with the thin lumen of the probe was the cause of more frequent extraction of the probe as in PEG. Other mild complication (convolution of the probe in stomach, dislocation of PEJ, infection of the dolg and syndrom of implanted target) occured in 10.41%, 12.5%, 4.2% a 2.1%. Frequency of these complication was comparable or lower to the literature. Hemorrhage didńt occure, as all patients had normal coagulative parameters and periprocedural drop-out of the antiagregative medication was done. Severe complication occurred in 2 patients: aspiratory pneumonia, complicated with death (3.2%) and peritonitis (3.2%), with lower frequency compare to the literature. Mortality accompanied with the procedure of in-patients is described in the literature in 25–29%. COPD was the predisposition factor of aspiration in our patient with the severe pneumonia, sepsis and multiorgan failure.

**Conclusion:** PEJ is the apropriate method for antiparkinsonic medication in the late stage of Parkinson's, if other options failed. We had less complications in comparison to the literature except of the obturation and removal of the probe. It is one of the newest indication of PEJ. It improves preservation of the motoric function and avoids to the progressive weight loss of the patients. Continual dosage of the treatment improves the neurologic state of the patients with Parkinson's disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0692 A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF VONOPRAZAN VS RABEPRAZOLE FOR GASTRIC ULCERS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Endoscopic submucosal dissection (ESD) for early stage gastric neoplasms was recently established in Japan. We usually use proton pomp inhibitors (PPIs) to prevent delayed bleeding after ESD and to induce rapid ulcer healing. Although many reports describe the healing of post-ESD ulcers by PPIs, there is no consensus for the optimal treatment. Recently, a potassium-competitive acid blocker (P-CAB), vonoprazan, has been developed in Japan. However, no study has reported the efficacy of vonoprazan in healing post-ESD ulcers.
**Aims & Methods:** The aim of this study was to compare the efficacy between P-CAB and PPI in healing post-ESD ulcers. This study was designed as a double-blind prospective randomized controlled trial (UMIN000017386). A total of 40 patients with gastric neoplasia (gastric cancer and adenoma) who were treated by ESD at our hospital from April 2015 to January 2016, were enrolled in this study. All patients were randomly assigned to two groups as follows: group A, vonoprazan 20 mg/day; group B, rabeprazole 10 mg/day before ESD; patients took these medications from a day before ESD to 4 weeks after ESD. They underwent esophagogastroduodenoscopy (EGD) after 4 weeks, and the ESD-induced artificial ulcer size was measured just after ESD and 4 weeks after ESD, to calculate the reduction rate. The ulcer reduction rate was calculated as area of ellipse: (ulcer area 4 weeks after ESD)/(ulcer area just after ESD) × 100 (%). In addition, gastric ulcer stage was classified using a 6-stage system Sakita-Miwa classification: active (A1, A2), healing (H1, H2), and scarring (S1, S2). We then compared group A and group B via a reduction rate and gastric ulcer stage.
**Results:** As a result, 18 cases in group A (13 males, 5 females; mean age 69 y), and 15 cases in group B (11 males, 4 females; mean age 70.9 y) were analyzed. No significant differences were observed in mean age, gender, BMI, comorbidity, *Helicobacter pylori* infection, and clinicopathological findings. There were significant differences in mean reduction rate (group A: 93.3%, from $741.3 \pm 666.8 \rightarrow$to $48.0 \pm 52.0 mm^2$; group B: from 96.6%,$1022.4 \pm 640.5 \rightarrow$to $31.0 \pm 19.1 mm^2$, $p < 0.01$). All gastric ulcers 4 weeks after ESD were classified as stage H1 or H2 (H1/H2; group A: 8/10; group B: 6/9), and there were no significant differences in gastric ulcer stage. Regarding the adverse events, post-ESD bleeding was observed in 5.6% of the patients (1/18) in group A, and drug-induced hepatic injury was observed in 6.7% of the patients (1/15) in group B.
**Conclusion:** Rabeprazole was significantly more effective than vonoprazan in healing after ESD ulcers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0693 DIFFERENTIAL DIAGNOSIS OF DIFFERENTIATED GASTRIC CANCER BY USING RAPID FLOW CYTOMETRY METHOD AS A CLINICAL APPLICATION

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**Introduction:** It is difficult to diagnose gastric cancer because of its various classifications and multiple criteria according to the facility. New approaches were developed to overcome the existing problems such as high resolution endoscopic camera technologies. However, the doctors still encounter the cases being difficult to diagnose, and have to wait for a few days to be ascertained the diagnosis by pathologists. Against this background, we focused on the flow cytometry technique that was much reported in 1980's.[1–3] Cell cycle analysis with flow cytometry was well known as a useful method to study cell division and proliferation in clinical specimens. On the other hand, there were some problems especially in sample preparation and technical requirement. Therefore, we proposed a rapid and simple procedure and an algorithm for quantitative analysis for clinical use.
**Aims & Methods:** 50 specimens taken during gastroendoscopy were measured with flow cytometry according to the previous study. [4] Each DNA histogram was analyzed with quantification method with the following parameters; "malignancy index", the integrated value of G0/G1, S, G2/M, and over G2/M,[5] then evaluated the correlation with the degree of tumor differentiation in 4 groups (normal, and poorly/ moderately/ well-differentiated). All procedures were performed at Tokyo Women's Medical University in 2015.
**Results:** The patient data were as follows; 22 males, 15 females, age from 30 to 94 y. o., 19 normal/ 12 poorly/ 7 moderately/ 12 well-differentiated tissues. Statistically significant differences were observed between well-differentiated and normal tissues ($p < 0.001$), meanwhile there was no difference between poorly or moderately-differentiated and normal tissues ($p = 0.3625$). The accuracy of the discrimination of well-differentiated tissues from normal tissues was 91.7% sensitivity and 90.5% selectivity. Since well-differentiated adenocarcinomas tend to derive homogeneously, it was easy to detect with flow cytometry technique, however, poor-prognosis cancers like poorly-differentiated adenocarcinomas were required higher sensitivity because of its infiltrating progression feature.
**Conclusion:** In this study, we demonstrated the possibility of discrimination of well-differentiated adenocarcinomas from normal tissues during gastroendoscopy using quaintitative flow cytometry method. Flow cytometry analysis has the potential to provide different aspect information of cells from histopathological investigation. We will continue collecting data and additionally evaluate correlation with the prognosis factors in future.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0694 OESOPHAGEAL ESD FOR BARRETT'S NEOPLASIA TAKES 9.9MIM/CM2 & DEPENDS ON THE LESION SIZE & CIRCUMFERRENTIAL EXTENSION OF THE NEOPLASIA

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**Introduction:** Endoscopic submucosal dissection (ESD) is superior to endoscopic mucosal resection(EMR) as it leads to en-bloc resection & reduces risk of recurrence. However, its uptake in the west has been limited due to long learning curve and procedure time. ESD in western hands takes long time and this has become a significant barrier in the adoption of this technique. We believe that if time taken to perform each individaul step of ESD can be established then future research can focus on developing devices which can shorten that time.
**Aims & Methods:** Aim: To establish individual component steps of ESD for Barrett's neoplasia & identify the time required for each component & factors predicting teh procedure time. Methods: A single, experienced, western Endoscopist performed all procedures for suspected Barrett's cancers >2 cm. All procedures were recorded in full on a digital recorder. First 30 procedures were considered as a part of learning curve and not analysed but all consecutive procedures after that were analysed by an independent researcher with knowledge of ESD. Lesion area was calculated based on length of the lesion and the percentage of the oesophageal circumference involved. Using the equation area-$= 2*\pi* r * l *\%$ circumferential involvement / 100. Here r = radius and l = length of lesion. The time for every component of the procedure was recorded: lesion

**Table 1 (P0694)**

| | Lesion evaluation (min) | SM injection | Mucosal incision | SM dissection | Accessory change | Haemostasis control | Post resection evaluation |
|---|---|---|---|---|---|---|---|
| Mean | 19 | 10.1 | 14.9 | 19.3 | 9.0 | 4.5 | 3.8 |
| Median | 20 | 8.9 | 14.8 | 15.5 | 9.2 | 3.9 | 3.8 |
| Range | 5.7–27 | 4.3–24 | 5.9–26.4 | 3.2–64.3 | 3.3–17.5 | 0.7–20 | 1.5–8 |
| | **24%** | **13%** | **18%** | **24%** | **11%** | **5%** | **5%** |

evaluation & marking, submucosal (SM) injection, mucosal incison, SM dissection, haemostasis & post-ESD site evaluation.
**Results:** ESD Component steps & time taken for each step. 29 consecutive videos were examined. All were Barrett's cancers (35% T-1b, 75% T-1a). The mean length was 30 mm (range:10–70 mm), with mean area of 8.2cm$^2$ (range:1.6–23cm$^2$). The mean procedure time was 81 mins (range:45–142 min), equating to 9.9 min/cm$^2$. The time taken for each component of the procedure is shown in Table 1. Only 42% of the time was spent in cutting (Mucosal incision and SM dissection). 24% of time was spent in evaluation and marking the margins. 24% of the time spent in changing accessories & injection. Procedure time was related to lesion area: 100 min for lesions $>10$cm$^2$ vs 72 mins for lesions $<5$cm$^2$($p=0.0056$). Circumferential extension had an effect, with $<25\%$ circumference taking 66 min vs 92 mins for lesions with $>25\%$ circumferential extension ($p=0.0025$)
**Conclusion:** Our data shows that it takes 9.9 min/cm$^2$ to perform ESD for Barrett's cancers. The time taken is directly related to the size and circumferential extent of the lesion. We also found that only 42% of the time is spent performing the actual resection and rest of the time is spent in supporting acts. This information can help focus the future research in reducing the ESD procedure time and also help plan appropriate time and remuneration for current ESD procedures. This data is unique to Barrett's neoplasia as identification of lesion margins is very challenging in Barrett's oesophagus and this is reflected in the fact that almost quarter of the time was spent doing that. Advances in imaging can help shorten this time.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0695 NEW ENDOSCOPIC FINDING OF ESOPHAGEAL ACHALASIA WITH ST SHORT HOOD: "CORONA APPEARANCE"

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**Introduction:** Detecting esophageal achalasia remains a challenge. We describe the diagnostic utility of "Corona appearance", a novel endoscopic finding specific to esophageal achalasia.
**Aims & Methods:** Following criteria had to be met during lower esophageal sphincter examination using the attached ST Hood short-type for positive Corona appearance: A) Congestion inside the hood, B) Ischemic change around the hood, and C) Palisade vessels outside the hood. Corona appearance and seven conventional endoscopic findings were compared for sensitivity and consistency ($\kappa$-value) among 53 untreated esophageal achalasia patients who underwent endoscopy at our hospital.
**Results:** Corona appearance had the highest sensitivity (91%; $\kappa$-value, 0.71). Other findings in descending order of sensitivity included 1) functional stenosis of the esophagogastric junction (EGJ; 86%; $\kappa$-value, 0.58), 2) mucosal thickening and whitish change (71%; $\kappa$-value, 0.27), 3) abnormal contraction of the esophageal body (59%; $\kappa$-value, 0.32), 4) dilation of the esophageal lumen (58%; $\kappa$-value, 0.53), 5) liquid remnant (57%; $\kappa$-value, 0.51), 6) Wrapping around EGJ (49%; $\kappa$-value, 0.14), and 7) food remnant (30%; $\kappa$-value, 0.88). Even in 22 patients with non-dilated achalasia (grade 1), corona appearance had highest sensitivity (88%) compared to other endoscopic findings ($\kappa$-value, 0.63).
**Conclusion:** Among endoscopic findings using a ST Hood short-type to diagnose esophageal achalasia, corona appearance had the highest sensitivity and its consistency ($\kappa$-value) among endoscopists was substantial compared to other endoscopic findings. Similar results were also seen in cases of non-dilated achalasia. Endoscopic diagnosis of esophageal achalasia with ST Hood short-type is very useful.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0696 FULL THICKNESS RESECTION DEVICE (FTRD): A NOVEL TOOL FOR COLONOSCOPIC ADENOMA RESECTION. FIRST CLINICAL EXPERIENCE FROM TWO TERTIARY REFERRAL CENTERS IN SWITZERLAND

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**Introduction:** Recently a novel endoscopic tool, the so-called "Full Thickness Resection Device" (FTRD, Ovesco, Germany), has been introduced. FTRD allows colonoscopic full thickness resection (FTR) of certain polyps that are not manageable by established techniques, especially non-lifting lesions measuring up to 30 mm in diameter. In addition, FTR is supposed to have a higher diagnostic accuracy in assessing depth of invasion in early cancer as compared to conventional endoscopic polypectomy techniques.
**Aims & Methods:** We report our first clinical experience with FTRD procedures, assessing technical success, completeness of resection (R0 status), rate of histologically proven FTR and safety. Methods: Retrospective analysis of 18 consecutive patients with colonic polyps treated with FTRD during the period of May 2015 through April 2016.
**Results:** 13 FTRD procedures were performed in the colon, 5 in the rectum. Indications were adenoma recurrence or residual adenoma with non-lifting sign after previous polypectomy (n = 7), treatment-naive adenoma with non-lifting sign (n = 5), staging resection following presumed incomplete polypectomy of early carcinoma (n = 5) and one adenoma located at the appendiceal orifice (n = 1). In one case (polyp at appendiceal orifice) the lesion could not be reached once the FTRD system was mounted, due to diverticulotic narrowing of the sigmoid. In the 17 remaining cases amenable to FTR, resection was en bloc and histologically complete (R0) in 94.1% (16/17) of patients. Complete FTR was achieved in 82.4% (14/17), i.e. 91.7% (11/12) in the colon and 60.0% (3/5) in the rectum. The mean diameter of resection specimens was 2.6 cm (range 1.8–3.2 cm). Two technical failures occurred in the initial phase of the study (one problem of handling, one malfunction of the device). Two post-procedure minor bleedings were seen (one requiring re-colonoscopy and adrenalin injection). Otherwise there were no complications during a one-month-follow-up.
**Conclusion:** According to these preliminary data, the novel technique of colonoscopic full thickness resection by FTRD appears to be feasible, efficacious and sufficiently safe in the treatment of non-lifting polyps of $\leq$30 mm in diameter. FTR is an adjunct to the armamentarium of established colonoscopic polypectomy techniques, as it offers minimally invasive treatment to a group of patients that would otherwise undergo surgery. Limitations include a lower rate of complete FTR in the rectum as compared to the colon. This has to be taken into account when dealing with dysplastic polyps or early carcinoma, where the purpose of FTR includes assessment of depth of invasion. Further prospective studies will have to corroborate this concept.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0697 IMPLEMENTATION OF AN OPTICAL DIAGNOSIS STRATEGY SAVES COSTS AND DOES NOT IMPAIR CLINICAL OUTCOMES OF A FIT-BASED CRC SCREENING PROGRAMME

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**Introduction:** With an optical diagnosis strategy, diminutive (1–5 mm) polyps throughout the colon are resected and discarded and diminutive recto-sigmoid hyperplastic polyps (HPs) are left in situ. Implementation of this strategy may result in reduced polypectomy-related complications, direct surveillance interval assignment and cost-savings. Previous modelling studies did not include the serrated neoplasia pathway, were based on primary screening colonoscopies and assumed a rather high percentage of high-confidence predictions. We evaluated the effectiveness and costs of an optical diagnosis strategy compared to polypectomy of all diminutive lesions followed by histopathological diagnosis.
**Aims & Methods:** The Adenoma and Serrated pathway to Colorectal Cancer (ASCCA) model was set up to simulate a biennial faecal immunochemical testing (FIT) screening programme, with referral to colonoscopy of FIT positives, as well as a primary colonoscopy screening programme in individuals aged 55 to 75 years. Surveillance colonoscopies were included in both screening scenarios. For each screening scenario, we compared a histopathological diagnosis strategy to an optical diagnosis strategy. In the latter strategy, diminutive HPs assessed with high-confidence located in the recto-sigmoid are left in situ and diminutive lesions throughout the colon assessed with high-confidence are not sent for histopathology. Based on recent literature, we assumed that 76% of optical diagnoses would be made with high confidence and that 88%, 91% and 88% of respectively adenomas, sessile-serrated polyps and HPs would be accurately characterized. Outcomes of each strategy included discounted life-years, costs and number of colonoscopies.
**Results:** The model predicted that in a FIT-screening programme with a strategy of histopathological diagnosis, 17 days of life are gained in the lifetime of a 20-year old individual compared to no screening. The optical diagnosis strategy led to similar health gains. In addition, it led to cost-savings compared to the histopathological diagnosis strategy. These cost-savings were mainly due to the lower percentage of colonoscopies with polypectomy in which histopathology was required. In the optical diagnosis strategy, histopathological analysis would be performed in $\sim$70% of diagnostic colonoscopies with polypectomy. In surveillance, only $\sim$40% of colonoscopies with polypectomy required histopathological evaluation. Projected to a fully implemented FIT screening programme in the Netherlands, this would result in yearly undiscounted cost-savings of $\sim$€2.5 million. The assigned surveillance intervals were comparable for both strategies. In colonoscopy screening, comparison of both strategies led to similar conclusions, although the additional cost-savings due to the optical diagnosis strategy were higher. This was mainly due to a lower proportion, i.e. $\sim$40%, of diagnostic colonoscopies with polypectomy in which pathology was required.
**Conclusion:** Based on the ASCCA model, an optical diagnosis strategy for diminutive polyps detected within a FIT-based or colonoscopy-based screening programme does not decrease the effectiveness of either screening strategy. However, implementation of this strategy can lead to economic benefits, especially in colonoscopy screening.
**Disclosure of Interest:** E. Dekker: Research equipment from Olympus on loan All other authors have declared no conflicts of interest.

## P0698 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF SUPERFICIAL COLORECTAL NEOPLASMS AT THE ANAL CANAL AND ILEOCECAL VALVE

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**Introduction:** Endoscopic resection of superficial neoplasms at the low perineal rectum is difficult due to pain sensibility, narrowness of the anal canal, presence of internal rectal plexus, whereas that of at the ileocecal valve (ICV) due to the various and variable morphology of the ICV itself and ileal involvement. These two anatomic locations are relative contraindications to the conventional endoscopic snare resection (EMR) even for non-invasive cancers due to a high incomplete resection rate. Aim was to assess the feasibility and outcomes of ESD of superficial neoplasms in the low rectum and ICV.

**Aims & Methods:** Retrospective analysis of prospectively collected database in a single nonacademic center. From 1.2010 to 7.2015, all consecutive patients scheduled to ESD for a superficial neoplasm in the low rectum (<10 mm from the dentate line) and at the ICV lip +/- ileal involvement, and no deep SM invasion (Kudo pit pattern type V; Sano microcapillary pattern type 3B) were included. ESD was performed with the standard technique. Follow-up was scheduled at 3 and 6 months within the first year and then yearly. Biopsies were taken from the scar of the resection site if a residual tissue was visible at chromoscopy and/or NBI.

**Results:** A total of 28 neoplasms (7 at ICV; 21 in the low rectum) underwent ESD (Table). Rectal neoplasms involved >50% of the circumference in 9 (43%) cases. Lesions at the ICV had a complete involvement of one lip in 4 (57%) cases and of the ileum for a median of 15 mm in 2 (29%) cases. ESD was en bloc in 22 (79%) with a median operating speed of 14 min/cm$^2$ (range 3–34), was converted to a piecemeal EMR in 5 patients, and incomplete in 1 residual neoplasm in the low rectum that underwent transanal microsurgery. Results according to neoplasm location are reported in the Table. ESD was R0 in 14 (50%) cases A delayed bleeding occurred in one rectal ESD. A curative ESD (comprising R1 due to lateral margins positive for dysplasia but no residue at follow-up) was achieved in 6 (86%) ICV and 14 (67%) rectal lesions. Three patients underwent additional surgery for high-risk pathologic features (2 after ESD, 1 after piecemeal EMR). During follow-up (median 12 months; range 12–32): no recurrence was observed in 14 R0-ESDs; a minute residue was observed in 1 (14%) /7 R1-ESDs and 1 1 (50%) /2 curative piecemeal EMR. An asymptomatic scar of anal canal was observed at digital rectal examination in 2 cases.

| | ICV (n.7) | Low Rectum (n.21) |
|---|---|---|
| size, mm (median, range) | 44 (20–85) | 48 (23–180) |
| morphology: LST-G / NG | 6 / 1 | 19 / 2 |
| scar (prev. resection) | 0 | 6 (29%) |
| ESD en bloc | 6 (86%) | 16 (76%) |
| ESD R0 | 3 (43%) | 11 /52%) |
| ESD R1 (LM / VM) | 3 / 0 | 4 / 1 |
| piecemeal EMR | 1 | 3 |
| T1 high-risk LN metastasis | 0 | 3 |

**Conclusion:** The ESD of large neoplasms at the ICV and in low perineal rectum involving the anal canal is feasible and effective. The complete resection rate is low due to the challenging anatomy of that precludes conducting a mucosal incision far from tumor margins. A careful endoscopic follow-up is mandatory but ESD (even when converted to piecemeal EMR) permitted to avoid incomplete endoscopic resections and unnecessary surgery.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0699 OPTIMIZING WITHDRAWAL TIME AND USE OF FUSE ENDOSCOPE ACHIEVE SIMILAR RESULTS IN TERM OF INCREASING ADENOMA DETECTION RATE. RESULTS OF A PRELIMINARY OBSERVATIONAL STUDY

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**Introduction:** Colonoscopy outcome is strictly related to the adenoma detection rate (ADR). An endoscopy withdrawal time (WT) >6 min has been suggested to increase the ADR since it allows for accurate evaluation of the several hidden areas of the colon. The FUSE endoscope has been demonstrated also to reduce the rate of missed lesions due to its wide angle view. In the present study we evaluate the impact on the ADR either of the use of a FUSE endoscope or of interventions directed at optimizing WT.

**Aims & Methods:** In a 3-month period 4 expert endoscopists performed 529 colonoscopies either with HD standard endoscope (SE) (n = 264) or with FUSE (n = 265) without a dedicated WT protocol. During a subsequent 2-month period they performed further 250 colonoscopies with standard scopes using dedicated inspection techniques and a minimum 6-minute WT. We compared overall rates of ADR in post-intervention procedures with those in baseline examinations.

**Results:** No differences were observed among the three groups in terms of demographic and clinical characteristics. Mean WT in the pre-intervention phase was 291+/-109 sec in the FUSE group and 260+/-94 in the SE group ($p < 0.01$). Introduction time was also longer for the FUSE (382 +/-187 sec vs 385 +/-184, $p < 0.02$). In the post-intervention phase WT increases to 386+/-69 sec ($p < 0.01$). In the pre-intervention the polyp detection rate was 60.7% (161/265) in the FUSE vs 48.1% (127/264) in the SE group ($p = 0.15$); in the post-intervention the polyp detection rate in the SE increases to 70% (175/250) ($p = 0.027$). Optimizing the WT, the ADR increases from 29.9% to 34.8% in the SE. The ADR achieved by the FUSE in the pre-intervention phase did not differ from the post-interventional ADR obtained by the SE (35.5% vs 34.8%, NS). Increase in the detection rate regarded exclusively small (<1 cm) polyps (40% in the SE pre-intervention group vs 47% in the FUSE group and 53% in the SE post-intervention group).

**Conclusion:** An intervention directed to optimize the withdrawal time determined in our series a significant increase in the number of detected lesions and a trend towards a better ADR. The same results were obtained by the FUSE scope independently of the withdrawal time. These preliminary results are likely to be important since use of FUSE may reduce the duration of colonoscopy without affecting its accuracy.

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## P0700 PREDICTORS RELATED TO COLONOSCOPY COMPLICATIONS IN AN ORGANISED COLORECTAL CANCER SCREENING PROGRAMME WITH IMMUNOCHEMICAL FAECAL OCCULT BLOOD TEST

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**Introduction:** Colorectal cancer (CRC) is a major cause of morbidity and mortality. CRC screening with biannual faecal occult blood test (FIT) has been shown to reduce CRC mortality. The efficacy of the screening programmes ultimately depends on the accuracy of post-FIT colonoscopy, however we must not underestimate the harms that they can produce.

**Aims & Methods:** Complications in a FIT screening programme occur from diagnostic colonoscopies after positive test results. The aim of this study is to determine which factors are related to these complications. Methods In 2009 the colorectal cancer screening programme started in the Basque Country, with a target population of 586,700 50 to 69 years-old citizens. This programme has a high participation rate (68.5%) and high colonoscopy compliance rate (93.1%). After a positive FIT result, patients underwent colonoscopy with sedation. Data of invitations from January, 2009 to December, 2014 on clinical characteristics of patients, screening history, endoscopic procedure and histology results were collected. Mortality and complications within 30 days after colonoscopy were identified through national registries and were assessed through the review of medical records. Predictors of colonoscopy complications were identified through a logistic regression.

**Results:** After 39,254 colonoscopies, complication rate was 1.1%. 70.4% were men and 61.7% 60–69 years-old. 83.4% had adequate bowel cleansing. 76% had an advanced adenoma (high risk adenoma or CRC). After a diagnostic colonoscopy, the risk of bleeding was 6/1,000 and the risk of perforation 2.8/1,000. The risk of post-polypectomy bleeding was 10/1,000 and perforation 4.6/1,000. No deaths had been reported. Independent predictors of colonoscopy complication were sex (OR:1.48 for men; 95%CI:1.03–2.14), history of abdominal surgery (OR:2.06; 95%CI:1.28–3.31), a colonoscopy performed in the previous 5 years (OR:30.77; 95%CI:4.13–229.32), diverticulosis (OR:2.79; 95%CI:1.84–4.23), polyp size ≥20 mm(OR:2.64; 95%CI:1.59–4.40) and advanced neoplasia in the diagnosis (OR:1.78; 95%CI:1.04–3.02). We found no relationship in: age, body mass index, anticoagulant or antiplatelet therapy and number of polyps removed. The area under ROC curve was 0.73 (95%CI:0.69–0.77). 88.1% of the patients with complications were admitted to hospital. 27.7% of them needed therapeutic colonoscopy and 10.1% surgical treatment. The average stay in hospital was 5 days (IQR: 3–7 days).

**Conclusion:** Colonoscopy, with or without removal of a lesion, is an invasive procedure with a small, but not insignificant risk of major complications. That is why, it is vital to know which aspects predict their appearance in order to implement according countermeasures.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0701 REAL TIME HISTOLOGY AT ENDOSCOPY – VIRTUAL ELECTRONIC CHROMOENDOSCOPY AND PROBE CONFOCAL LASER ENDOMICROSCOPY CAN ASSESS SUBTLE MUCOSAL AND VASCULAR INFLAMMATORY CHANGES IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** Inflammation is considered increasingly important in the assessment of disease activity and therapeutic response in ulcerative colitis (UC). Histological assessment is being standardized to reflect disease activity even when endoscopic features are subtle. We have reported that such subtle changes can be detected by iSCAN virtual electronic chromoendoscopy (VCE) scoring.[1] Probe confocal laser endomicroscopy (pCLE) is an endoscopic tool which allows real time histology of mucosa therefore may provide histology- like images.

**Aims & Methods:** We aimed to determine whether pCLE reflected VCE and the mild –chronic subtle changes histological abnormalities in UC patients compared with the newly defined histological ECAP score,[1] and the recently validated Robarts Histology Index (RHI).

**Patients & Methods:** 90 patients (82 UC and 8 Controls) (Male: 54, median age 47 years; Range 19–79 y) were assessed with high definition –iSCAN virtual chromoendoscopy (HD-VCE)(Pentax, Japan) and pCLE (Cellvizio, Paris) after IV fluorescein. The endomicroscopy findings were graded as A) Crypt architecture: (1) normal, (2) irregular, (3) drop-outs, (4) cryptitis, (5) necrosis with crypt abscess; B) Leakage of fluorescein: (1) normal, (2) low density in the lumen of the crypts, (3) among the cells, (4) high density in the lumen of the crypts;C) Vessel architecture: (1) normal, (2) branchless, (3) tortuous, (4) dilated; D) Blood flow: (1) normal, (2) low back and forth flow, (3) high back and forth flow, (4) stagnant. Harpaz grade, the newly ECAP[1] score and the validated Robarts Histology Index (RHI) were used to represent the histological acute and chronic changes of inflammation.

**Results:** The Mayo endoscopy subscore was significantly correlated with pCLE score (rs = 0.79, 95%CI 0.7–0.85; $p < 0.001$). The overall mucosal and vascular pattern iSCAN endoscopic score[1] was significantly correlated with pCLE score (rs = 0.83, 95%CI 0.76–0.88; $p < 0.0001$). pCLE features of leakage of fluorescein (rs = 0.75, 95%CI 0.64–0.87; $p < 0.00001$), vascular architecture (rs = 0.77, 95%CI 0.67–0.84; $p < 0.0001$) and blood flow (rs = 0.80, 95%CI 0.71–0.86; $p < 0.00001$) reflected the endoscopic iSCAN vascular pattern. The Harpaz histology score was correlated with pCLE (rs = 0.59,95%CI 0.44–0.71; $p < 0.0001$). The RHI was also correlated with pCLE (rs = 0.60,95% CI 0.45–0.72; $p < 0.001$). The ECAP score correlated better with pCLE score (rs = 0.70, 95% CI 0.58–0.79; $p < 0.0001$).

**Conclusion:** pCLE can assess grade of inflammation in UC patients, both at VCE and histology levels. The leakage of fluorescein, vessels architecture and blood flow determined by pCLE reflect well the vascular changes seen by VCE. Technological advances in endoscopy are rapidly approximating histology in intestinal inflammation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0702 DIAGNOSTIC ACCURACY OF THE NICE CLASSIFICATION FOR PREDICTING DEEP SUBMUCOSAL INVASION IN COLON LESIONS ASSESSED IN VIVO. PRELIMINARY RESULT

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**Introduction:** The prediction of deep submucosal invasion in a colon polyp is a challenge and an important factor in the choice of the best and safest treatment. The NICE classification attempts to resolve this issue, but it has not been validated in vivo.

**Aims & Methods:** Prospective, observational study to assess diagnostic accuracy of the NICE classification for predicting deep submucosal invasion ($>1000\,\mu m$) in polyps $>1$ cm detected during colonoscopies in routine clinical practice. Forty-five endoscopists from 14 Spanish hospitals included all consecutive colonic lesions type 0 in the Paris classification and larger than 1 cm. Characteristics of the patients and the lesions were recorded. Primary outcomes were the diagnostic test (NICE classification: 1/2/3) and the gold standard (blinded histology evaluation based on the Vienna classification). In addition, the degree of confidence of the assessment of the NICE classification (high/low) was also recorded. NICE categories 1 and 2 were grouped in a single category (non-NICE 3) in the statistical analysis. Lesions with deep submucosal invasion evaluated as NICE 3 were considered true positives, and lesions with non-deep

**Table 1. (P0702):** Diagnostic accuracy of NICE classification to predict deep submucosal invasion according to the confidence and morphology

| | N lesions | P of DSI | Se, % (95%CI) | Sp, % (95%CI) | PPV, % (95%CI) | NPV, % (95%CI) |
|---|---|---|---|---|---|---|
| Overall | 846 | 1.3 | 54.5 (51–58) | 95 (94–96) | 12.5 (10–15) | 99.4 (99–100) |
| Confidence | | | | | | |
| High | 760 | 0.9 | 57.1 (54–61) | 97.7 (97–99) | 19 (16–22) | 99.6 (99–100) |
| Low | 86 | 4.6 | 50 (39–61) | 69.5 (60–79) | 7.4 (2–13) | 96.6 (93–100) |
| Morphology and condifence | | | | | | |
| Non-0-Ip | 524 | 1.9 | 60 (56–64) | 94.7 (93–97) | 18.2 (15–22) | 99.2 (98–100) |
| High | 463 | 1.3 | 66.7 (62–71) | 97.8 (97–99) | 28.6 (25–33) | 99.5 (99–100) |
| Low | 61 | 6.6 | 50 (37–62) | 70.2 (59–82) | 10.5 (3–18) | 95.2 (90–100) |
| 0-Ip | 322 | 0.3 | 0 | 95.3 (93–98) | 0 | 99.7 (99–100) |
| High | 297 | 0.3 | 0 | 98 (96–99) | 0 | 99.7 (99–100) |
| Low | 25 | 0 | - | 68 | - | - |

P: prevalence; DSI: deep submucosal invasion

submucosal invasion evaluated as non-NICE 3 were considered true negatives. Sensitivity (Se), Specificity (Sp), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated. Subanalyses were performed in high/low confidence lesions and in pedunculated (0–Ip)/non-pedunculated lesions, because the significance of deep submucosal invasion in 0–Ip lesions is uncertain.
**Results:** Nine hundred and two lesions (620 patients) were included (50% of the needed sample). Seventeen pT1 awaiting for a specific histological assessment were excluded at the moment. In addition, therty-nine lesions were also excluded for other reasons. Se, Sp, PPV and NPV were 54%, 95%, 12% and 99%. Diagnostic accuracy according to the grade of confidence and the lesions' morphology is shown in table 1.
**Conclusion:** This intermediate analysis shows that the Specificity and Negative Predictive Value of the NICE classification for predicting deep submucosal invasion in routine clinical practice are high. However, Sensitivity and Positive Predictive Value did not achieve acceptable levels. We must wait for the final results to better assess its role in routine clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0703 VALIDATION OF ENDOSCOPIC CLASSIFICATION FOR COLORECTAL LATERALLY SPREADING TUMORS USING AN EDUCATIONAL WEBSYSTEM

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**Introduction:** Classification of the Laterally Spreading Tumors (LSTs) in the colon and rectum can be useful to predict the risk of containing submucosal invasion. In turn, pre-treatment diagnosis can guide the therapeutic plan: EMR, ESD or surgery. Development of a universal classification of the LSTs is needed for worldwide collaboration. We examined the interobserver agreement (IOA) for classification of LSTs among international experts as a first step towards validation and wide implementation in practice.
**Aims & Methods:** We developed an educational, web-based system to classify the endoscopic aspect of LSTs, using a modified Delphi process. We defined LSTs as large (≥10 mm) laterally superficial growing lesions. We included in the web-based system still images of LSTs using high-definition white-light endoscopy and chromoendoscopy (indigo carmine dye spraying). We asked raters to classify the lesions according to two standardized classifications: A. Kudo Classification, which included granular homogenous (LST-G-H) type; granular nodular mixed (LST-G-NM) type; non-granular flat-elevated (LST-NG-FE) type; or non-granular pseudodepressed (LST-NG-PD) type; and B. Paris classification, which included: Ip, Is, IIa, IIb, IIc and combinations. Raters were blinded to histopathology. We calculated the interobserver agreement (IOA) using Fleiss kappa coefficients with 95% confidence intervals and the proportion of pairwise agreement. Sensitivity analyses were performed to adjust for high impact of single raters.
**Results:** A total of 72 cases were assessed by 13 international (7 Western and 6 Eastern) experts. Overall, there is good interobserver agreement (IOA) for Kudo classification of LSTs into granular vs non-granular type (Fleiss kappa: 0.76 [0.72–0.79], pairwise agreement: 88.2%). The IOA varies by endoscopic type, with good IOA (kappa: 0.76 [0.68–0.84]) for LST-G-NM type vs moderate agreement (kappa: 0.54 [0.47–0.61]) for LST-NG-PD type. The IOA for Paris classification is only moderate (kappa: 0.51 [0.45–0.57], pairwise agreement: 73.5%). The IOA improves with lesion size (kappa: 0.64 for LST ≥30 mm vs kappa: 0.53 for LSTs <30 mm) and improves along the study (from kappa: 0.53 for the first third of cases to kappa: 0.68 for the last third of cases). In total, there were 50 adenomas, 4 early carcinomas and 18 sessile serrated adenomas/polyps. IOA did not differ by histopathology.
**Conclusion:** Using an educational web-based system, a good interobserver agreement was achieved among international experts in classifying colorectal LSTs into granular vs non-granular type. Interobserver agreement was highest for LST-G-NM type and lowest for LST-NG-PD type. Endoscopic classification of LSTs helps to standardize their management to optimize outcomes. Additional training is therefore required to implement the LST classification widely in clinical practice.
**Disclosure of Interest:** S. Sanduleanu: Consultancy: Pentax Medical Systems Europe
All other authors have declared no conflicts of interest.

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### P0704 COLORECTAL POLYPS DIAGNOSIS BY NARROW-BAND IMAGING – DIFFERENCES BETWEEN THE CLINICAL TRIALS AND THE REAL WORLD

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**Introduction:** Studies with highly experienced endoscopists revealed a moderate to high accuracy of Narrow-band imaging (NBI) in real time histological characterization of colorectal polyps. Its implementation in the real world remains to be determined, particularly in diminutive polyps (≤5 mm), for which recent guidelines propose "resect and discard" and do "not resect" (for rectosigmoid polyps) strategies.
**Aims & Methods:** To assess the role of NBI for predicting histology of colorectal polyps, using the NICE (NBI-International Colorectal Endoscopic Classification) and WASP classifications (Workgroup Serrated Polyps and Polyposis). Prospective, single-center study of patients undergoing elective colonoscopy (colonoscope CF-H190®, Olympus) between January-February 2016. Colonoscopies were performed by endoscopists with no prior NBI experience, except for a 20-minutes interactive session. Polyp characteristics were recorded: location, size, morphology (Paris classification), NICE/WASP classifications (1p-hyperplastic, 1s-sessile serrated, 2-adenoma, 3-deep submucosal invasive carcinoma) and confidence level in this classification (low: <90% vs high: >90%). Polyp histology was determined by anatomo-pathologists blinded to the NICE/WASP diagnosis. Statistics: Fisher's exact test, logistic regression (SPSS-21).
**Results:** 207 polyps of 95 patients were evaluated; average size 6.3 mm (2–35 mm); 71% 0–Is; 59.4% in the left colon. Histology: hyperplastic polyp −26.6% (n = 55), sessile serrated adenoma −4.3% (n = 9), adenoma −61.4% (n = 127), adenocarcinoma −0.5% (n = 1), inflammatory polyps/normal mucosa −7.2% (n = 15). Type of polyp according to NICE/WASP classifications: 1p – 32.9% (n = 68), 1s – 7.7% (n = 16), 2–59.4% (n = 123). The diagnosis of adenoma by NICE/WASP classifications presented an accuracy, sensitivity, specificity, positive predictive value and negative predictive value of 76.8%, 72.5%, 79.5%, 82.0% and 68.2%, respectively. For polyps ≤5 mm, located on the left colon (n = 76) there was better accuracy (81.3%), with 73.3% of the predictions made with a high confidence level. In multivariate analysis the high level of confidence (p = 0.010) and <3 polyps resected/exam (p = 0.042) were associated with the correct classification by NBI.
**Conclusion:** The application of NBI by inexperienced endoscopists showed moderate accuracy in histology prediction. For diminutive polyps of the left colon, the accuracy and confidence levels were lower than the thresholds recommended by the ASGE guidelines (≥90%). These results justify additional training and monitoring.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0705 COLONOSCOPIC FINDINGS IN PATIENTS WITH INCIDENTAL COLONIC FOCAL FDG UPTAKE

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**Introduction:** The relevance of incidental colorectal focal FDG-PET/CT uptake is debatable. The aim of this study was to investigate the nature of FDG-avid and non-FDG-avid lesions detected at colonoscopy in patients presenting with incidental focal uptake.

**Aims & Methods:** Charts of patients without known history of colorectal disease, who were referred in our endoscopy center for lower GI endoscopic evaluation of incidental colonic focal FDG uptake, were retrospectively reviewed. Patients with segmental or diffuse uptake were excluded. Characteristics of PET/CT images were assessed by a nuclear physician blinded to endoscopic and histopathologic findings to localize FDG uptake and measure maximum standardized uptake values (SUVmax). Endoscopic findings and histologic results were categorized into malignant lesions (adenocarcinoma), high-risk polyps (HRP, polyp $\geq$ 10 mm, with high-grade dysplasia for adenoma, or dysplasia for sessile serrated polyp), low-risk polyps (LRP, adenoma or sessile serrated polyp) or other non neoplastic lesions (NNL, hyperplastic polyps, or various lesions). The colon was divided into 4 segments: rectosigmoid, left, transverse, and right colon. Analyses per-patient, per-FDG uptake and per-lesion were performed. Kruskall Wallis test was used for comparison.

**Results:** From 2005 to 2015, 82 consecutive patients with incidental colonic uptake were referred for colonoscopy. Twelve patients with segmental or diffuse uptake were excluded; 84 focal areas of FDG uptake were detected in the 70 included patients. Colonoscopy was total in 52 (74.3%) and incomplete in 18 patients. The colonic segments with FDG uptake were constantly assessed by colonoscopy and a total amount of 233/280 (83.2%) colonic segments were evaluated with colonoscopy. Among the 84 focal areas, 43 (51.2%) were in the rectosigmoid, 12 (14.3%) in the left colon, 9 (10.7%) in the transverse colon, and 20 (23.8%) in the right colon. The proportions of true-positive (lesion found at colonoscopy at the same location) and false-positive (no lesion at colonoscopy) PET/CT results were 55 (65.5%) and 29 (34.5%). SUVmax values differed significantly between true-positive ($11.4 \pm 0.79$) and false-positive ($8.5 \pm 0.94$) FDG-uptakes ($P < 0.02$). The area under the curve was 0.63. The optimal cut-off SUVmax was 8.9 (sensitivity 55%, specificity 75%). The number of lesions seen at colonoscopy and the number of colonic segments with lesions were 107, and 83, respectively. Among the 83 colonic segments with lesion seen at colonoscopy, FDG-uptake was present in 52 cases and absent in 31 cases. Among the 150 colonic segments without any lesion, FDG-uptake was present in 25 cases and absent in 125 cases. Thus, the distribution of true-positive, false-negative, false-positive, and true-negative FDG-PET/CT results were 22.3%, 13.3%, 10.7%, and 53.7%. Among the 55 true-positive FDG uptakes, there were 14 (25.5%) malignant lesions, 30 (54.5%) HRP, 4 (7.3%) LRP, and 7 (12.7%) NNL. SUVmax did not differ significantly between groups according to histopathologic diagnosis ($p = 0.8$). The 34 non-FDG-avid lesions detected in 31 colonic segments corresponded to 5 (14.7%) HRP, 27 (79.4%) LRP and 2 (5.9%) NNL.

**Conclusion:** Our study demonstrates that two-thirds of sites of FDG uptake correspond to a lesion at colonoscopy and 52% of FDG uptake to advanced neoplasia. Although mean SUVmax values are significantly higher in true-positive than false-postive FDG uptake, individual values did not correlate with histopathologic diagnosis. The majority of non-FDG-avid lesions corresponded to LRP. We conclude that incidental focal colonic FDG uptake should be evaluated by total colonoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0706 ENDOSCOPIC REMOVAL OF EARLY STAGE COLORECTAL CANCER IN A FIT-BASED SCREENING POPULATION: PROGRESS STILL TO BE MADE

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**Introduction:** Endoscopic recognition and resection of early colorectal cancers (CRCs) is likely to influence the efficacy of CRC screening programs. Patient survival after (endoscopic) resection of early CRC confined to the superficial layers is higher compared to more advanced lesions and prevents a more invasive surgical resection. Literature concerning identification and endoscopic removal of early CRC in a screening setting is limited.

**Aims & Methods:** We therefore assessed if endoscopically resectable CRCs are identified correctly at colonoscopy within the framework of a fecal immunochemical tests (FIT)-based CRC screening program, and what the final treatment and outcomes of these patients were. A random sample of 13,566 persons from the Dutch general population, aged 50–74 years, were invited to participate in a FIT-based screening program, between November 2006 and October 2014. Participants were referred for colonoscopy in case of a positive FIT (cut-off $\geq$10 µg hemoglobin per gram feces). From all detected CRCs, we included endoscopically resectable cancers, defined as a CRC confined to the submucosa, without invasion of the muscularis propria or deeper wall (T1N0M0). Endoscopic resections were considered sufficient, in case of an R0 resection and resection margin $>$1 mm. Dutch guidelines were followed for treatment and surveillance recommendations, which are comparable to American Society for Gastrointestinal Endoscopy guidelines.

**Results:** Twenty patients were diagnosed with a histologically proven T1N0M0 malignant colorectal polyp. These cancers had a median size of 16 mm (range 5–40 mm) and were located in cecum (n = 1), ascending colon (n = 3), descending colon (n = 1), sigmoid (n = 13) and rectum (n = 2). Seven (35%) polyps were identified as potentially malignant before resection based on its endoscopic appearance (table 1). In total, sixteen (80%) primary endoscopic resections were performed and four (20%) primary surgical resections. Reasons for primary surgical resections were (incorrect) suspicion of stadium T2 or more by the endoscopist (n = 3) and familial adenomatous polyposis (n = 1). R0 resection rate with resection margin $>$1 mm, was 50% in the identified CRCs at colonoscopy and in 33% of the non-identified CRCs. Five (71%) patients from the endoscopically identified CRCs underwent surgery and six (46%) from the non-identified CRC (table 1).

**Table 1:** Endoscopy results and additional surgery after diagnosis of endoscopic resectable colorectal cancers detected by FIT in a CRC screening population.

| | IdentifiedCRC n = 7 | Non-identifiedCRC n = 13 |
|---|---|---|
| **Endoscopy** | | |
| Endoscopic resection (n,%) Yes No | 4 (57) 3 (43) | 12 (92) 1* (8) |
| **Endoscopic resection method (n,%)** | | |
| **ESD Liscoagulation Piecemeal Not described** | 2 2 3 | 8 2 2 |
| **En bloc resection (n,%)** | (n = 4) | (n = 4) |
| **Yes No** | 4 (100) | 4 (33) 8 (67) |
| **R0 resection and margin $>$1 mm (n,%)** | (n = 4) | (n = 12) |
| Yes No | 2 (50) 2 (50) | 4 (33) 8 (67) |
| Surgical resection performed (n,%) | | |
| Yes No | 5 (71) 2 (29) | 6 (46) 7 (54) |
| **Reason surgical resection (n)** | | |
| **Suspicion of stadium T2 or moreEndoscopic resection margin not free or $<$1 mm Lymphovascular invasionEndoscopic piecemeal resectionPerforation during endoscopy FAP** | 3 1 1 | 2 2 1 1* |
| **Tumour found in resection preparation (n,%)** | (n = 5) | (n = 6) |
| Yes No | 4 (80) 1 (20) | 1* (17) 5 (83) |

*Patient diagnosed with FAP at initial colonoscopy. In this patient a colectomy was performed subsequent to the initial colonoscopy and in the resected colon a T1N0M0 CRC was found.

**Conclusion:** In this FIT-based CRC screening population, more than half of the endoscopically resectable CRCs were not identified as such during initial colonoscopy. Additional surgery was still required in a substantial part of these patients often due to incomplete and undetermined resection margins. Our findings implicate that improvement in the recognition of early CRC and use of endoscopic resection techniques are mandatory to ensure completeness for proper pathological evaluation and staging.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0707 FULL SPECTRUM ENDOSCOPY (FUSE) VERSUS STANDARD FORWARD VIEWING ENDOSCOPE (SFVE) IN A HIGH-RISK POPULATION

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**Introduction:** Identifying polyps and subsequent polypectomy of adenomas during screening colonoscopies can prevent colorectal cancer (CRC). High adenoma detection rates (ADR) correlate inversely with the risk of interval cancers(1), making ADR the most important quality indicator in colonoscopy. Promising results have been seen with the use of Full Spectrum Endoscopy (FUSE) colonoscope in terms of ADR, but data from a high risk population is limited.

**Aims & Methods:** The purpose of the study was to investigate the diagnostic performance of FUSE compared to a conventional forward viewing endoscope. The primary outcome was CRC detection and ADR. Secondary outcome was

feasibility of FUSE opposed to Olympus standard forward viewing colonoscope (SFVE). 205 consecutive patients participating in the Danish CRC screening program were prospectively included in the study. Participants underwent FUSE colonoscopy on days when the FUSE system was available, while the remaining participants had SFVE. Baseline characteristics in terms of age, gender, ASA score, BMI, anticoagulation/antiplatelet therapy, 1st degree familiar history of CRC, prior colon resection and prior laparotomy were recorded. Following procedural parameters were recorded: completion rate, cecal intubation time, fentanyl and midazolam sedation, CRC detection, ADR, diverticulosis, bowel preparation, patient discomfort and endoscopist difficulty rating. All colonoscopies were performed by two trained endoscopists. Data were analysed using Student t-test, Fishers Exact test, Chi-squared test and Wilcoxon rank sum test.

**Results:** 109 patients were included in the FUSE group and 106 in the SFVE group. Mean age was $64.3 \pm 8.3$ and $64.5 \pm 8.0$ years, 51.4% and 50.0% were male, mean BMI $25.7 \pm 4.5$ and $26.1 \pm 4.5\,kg/m^2$ in the FUSE group and SFVE group, respectively. The two groups were comparable in age, gender, BMI, ASA score, anticoagulation/antiplatelet therapy, 1st degree familiar history of CRC, prior colon resection and prior laparotomy. Completion rate was 18/109 with FUSE and 7/106 in with SFVE ($p = 0.040$). Incompletion was due to pain in 6 vs. 1 ($p = 0.119$), preparation 6 vs. 5 ($p = 1$), malignant stricture 2 vs. 0 ($p = 0.498$), benign stricture 2 vs. 0 ($p = 0498$) and other 2 vs. 1 ($p = 1$) with FUSE and with SFVE respectively. Cecal intubation time was $11.4 \pm 6.7$with FUSE and $9.1 \pm 6.2$ with SFVE ($p = 0.042$, adjusted for bowel preparation, prior surgery, diverticulosis and BMI). CRC detection was 8.5% and 3.0% ($p = 0.126$), ADR was 67.0% and 59.6% ($p = 0.362$), while total adenoma detection was 166 (1.82/patient) and 139 (1.40) ($p = 0.094$) with FUSE and with SFVE respectively. No difference in patient discomfort ($p = 0.781$) was recorded between the two groups. Significant difference in difficulty rating among endoscopists was observed with FUSE compared to SFVE ($p > 0.001$).

**Conclusion:** There is tendency that FUSE colonoscopies identifies a greater number of adenomas compared to SFVE in a CRC screening population. Nonetheless, FUSE colonoscopies has a lower completion rate, longer cecal intubation time and a higher difficulty rating from an endoscopist point of view.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0708 1 L MORNING-ONLY POLYETHYLENE GLYCOL PLUS ASCORBIC ACID WITH PREPACKAGED LOW-RESIDUE DIET VERSUS 2L POLYETHYLENE GLYCOL PLUS ASCORBIC ACID FOR BOWEL PREPARATION: A RANDOMIZED TRIAL

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**Introduction:** 2L polyethylene glycol plus ascorbic acid (PEGA) is known to be as effective as standard 4L polyethylene glycol for bowel preparation. However, the volume of this regimen is still large to ingest. Therefore, we evaluated the potential of 1L PEGA with prepackaged low-residue diet (PLD) for an alternative to 2L PEGA. We report the interim results of this ongoing study.

**Aims & Methods:** The subjects were randomly assigned either to PEGA group or PLD group ($n = 100$ for each group). PEGA group received 2L PEGA (a split regimen for morning colonoscopy and a same-day regimen for afternoon colonoscopy). PLD group received PLD on the day preceding colonoscopy and 1L PEGA on the morning of colonoscopy. A questionnaire regarding bowel preparation was administrated on the morning of colonoscopy by telephone. One blinded endoscopist performed colonoscopy and evaluated the degree of bowel preparation using Boston bowel preparation score (BBPS).

**Results:** A total of 128 patients (male 56.3%, mean age 56) completed this study (68 in PEGA group, 60 in PLD group). There was no significant difference in the baseline characteristics such as sex, age, history of abdominal surgery, body mass index, and indication for colonoscopy between the two groups. The palatability of PLD was acceptable (bad taste 6.8%). The proportion of subjects who are willing to undergo colonoscopy with the same bowel preparation regimen used in the present study was higher in PLD group than in PEGA group (96.6% vs. 29.9%, $p < 0.001$). Although total BBPS was significantly higher in PLD group than in PEGA group (median 9 vs. 8, $p = 0.005$), the proportion of adequate bowel preparation (BBPS > 4) was not different between PEGA and PLD groups (98.5% vs. 96.6%, $p = 0.599$). There were no difference in the cecal intubation rate (98.5% vs. 98.3%, $p = 1.0$), cecal intubation time (median 240 seconds vs. 280 seconds, $p = 0.230$), and adenoma detection rate (40.3% vs. 42.4%, $p = 0.857$) between PEGA and PLD groups.

**Conclusion:** 1L PEGA with PLD showed similar efficacy for bowel preparation to 2L PEGA and higher acceptability than 2L PEGA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0709 A NEW DEVICE FOR ACHIEVING ADEQUATE BOWEL PREP IN POORLY PREPPED PATIENTS RECEIVING A REDUCED PRE-PROCEDURAL PREPARATION

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**Introduction:** Colonoscopy is the gold standard for evaluating the colon and an effective bowel preparation is essential to perform a quality colonoscopy. Inadequate preparation, estimated as many as 25% of colonoscopy procedures, results in increased rates of missed lesions, earlier repeat procedures, prolonged colonoscopy duration, reduced patient satisfaction and increased costs The MOTUS GI Pure-Vu™ System (Tirat Carmel, Israel) has been designed to improve visualization in an inadequately prepared colon by facilitating intra-procedural cleaning. The Pure-Vu system consists of a disposable single-use over-sleeve and a supporting workstation controller. The disposable over-sleeve fits easily on standard colonoscopes and does not interfere with the working channel or the navigation and advancement of the colonoscope. A foot pedal accessed by the physician controls the workstation to deliver irrigation jets to cleanse and evacuation to effectively remove considerable colon content.

**Aims & Methods:** Fifty procedures from two clinical sites using identical protocols, Carmel Medical Center in Haifa, Israel ($N = 9$) and San Rafael Hospital in Cadiz, Spain ($N = 41$), used the Pure-Vu System in partially prepped patients receiving a colonoscopy for screening, diagnostic or surveillance. The preparation used to ensure an inadequately prepped colon included a spilt dose of two tablets of 5mg Bisacodyl/ Laxadin, diet restrictions (no dried fruit, seeds or nuts) starting 2 days before the procedure and a 24 or 18 hour clear liquid diet prior to the colonoscopy. At 2 and 14 days post procedure a telephone follow-up was conducted to assess patient well-being and capture any adverse events. The study endpoints were: (1) improvement of colon cleansing level as per the Boston Bowel Preparation Scoring (BBPS) when comparing before and after Pure-Vu use, (2) Pure-Vu usability via questionnaire and (3) safety.

**Results:** Fifty subjects (64% males) are included in this analysis. The subjects' age ranges from 26–73 years, and their average BMI was 26. Results were analyzed on both a Per Protocol (PP) and Intent To Treat (IIT) basis due to patient non-compliance with the pre-procedural prep regime The Pure-Vu significantly reduced the number of subjects with an inadequate cleansing level (BBPS score < 2 of at least one colon segment). As per PP analysis, the rate of inadequate cleansing rate improved from (34/49) 69% at baseline to (1/49) 2% after use of Pure-Vu ($p < 0.001$), The mean and standard deviation of the post-treatment BBPS score was $2.96 \pm 0.29$. The cecum was reached successfully in (48/49) 98% of the cases. As per IIT analysis, the rate of adequate cleansing level pre and post procedure was 30% and 96%, respectively. The physicians were satisfied with the device's ease of advancement and found it easy to use and intuitive to operate. No serious adverse events were reported.

**Conclusion:** The Pure-Vu System was found to be simple, safe and effective in cleaning inadequately prepared colons to an adequate level for a thorough exam. Based upon these early results the device is expected to have a role in subjects with an inadequately prepared colon which may help to improve overall quality of colonoscopy, reduce the need to cancel or repeat colonoscopy procedures and improve patient satisfaction by reducing the burden of prep especially in those patients that have difficulty tolerating current prep regimes.

**Disclosure of Interest:** O. Segol: share company options
All other authors have declared no conflicts of interest.

### P0710 ACCURACY OF THE FULL SPECTRUM ENDOSCOPY SYSTEM (FUSE) FOR PREDICTION OF COLORECTAL POLYP HISTOLOGY ACCORDING TO THE REQUIREMENTS OF THE PIVI STATEMENT

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**Introduction:** In contrast to other endoscopy systems, FUSE uses LEDs to illuminate the tissue, thereby potentially providing more contrast as xenon lamps which emits over a broad spectrum across the visible range. The ASGE PIVI statement proposed that a new technology should provide a negative predictive value (NPV) >90% for adenomatous polyp histology to leave distal diminutive colorectal polyps in place without resection. To our knowledge no prior study has yet evaluated the feasibility of the recently introduced FUSE system for real-time in vivo prediction of polyp histology.

**Aims & Methods:** Prospective assessment of real-time prediction of colorectal polyps by using the FUSE System. Therefore, consecutive patients undergoing screening or surveillance colonoscopy were included. Colorectal lesions were evaluated in real-time by using the FUSE system. Before resection, the endoscopist described each polyp according to size, shape and surface characteristics (pit and vascular pattern, color, depression) and histology was predicted with a level of confidence (high or low).

**Results:** The histology was predicted with high-confidence in 87.6% of polyps. The overall accuracy for prediction of adenomatous polyp histology was 95.6% with sensitivity, specificity, positive and negative predictive value of 97.8%, 87.5%, 96.7%, and 91.3%, respectively. When the prediction was made with high-confidence, the accuracy was 96.9%. Sensitivity, specificity, positive and negative predictive values were 98.8%, 89.5%, 97.5%, and 94.4%, respectively.

**Conclusion:** The FUSE system is accurate enough for in vivo prediction of colorectal polyp histology. These findings need to be evaluated in future prospective, controlled, and blinded clinical trials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0711 EFFECT OF THE MAGNETIC ENDOSCOPE IMAGER ON COLONOSCOPY PERFORMANCE BY A SINGLE ENDOSCOPIST

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**Introduction:** Colonoscopy is the gold standard investigation for colonic assessment. To maintain clinical excellence in colonoscopy several performance indicators are recognised[1]. Colonic looping is a common patient-related factor which may reduce completion rates. The magnetic endoscope imager (MEI), a device which generates a three-dimensional map of colonoscope orientation, provides feedback regarding tip location and loop formation. MEI may improve colonoscopy outcomes however findings are inconsistent.
**Aims & Methods:** This study aimed to evaluate whether MEI use improves outcomes in colonoscopy completed by a single endoscopist. This retrospective cohort study investigated the effect of MEI on procedure completion, polyp detection, medication doses (sedation, analgesia and buscopan), endoscopist and nurse discomfort scores and patient satisfaction in patients undergoing colonoscopy. Data was obtained by interrogation of electronic colonoscopy records for a single gastroenterologist between December 2009 and November 2014. The equipment used for all colonoscopies was identical in make and age, the only difference being the presence or absence of the MEI. Statistical analysis was completed using Wizard©.
**Results:** 2129 colonoscopies were completed during the study period across three endoscopy units. After exclusion of incomplete data, study groups significantly differed by age demographics. By excluding patients older than 74 y, study groups ($n = 914$ without MEI, $n = 359$ with MEI) had similar age ($p = 0.06$) and gender ($p = 0.962$) characteristics. MEI use did not significantly influence colonoscopy completion (97.2% vs 96.3%, ($p = 0.412$)) or polyp detection (24.8% vs 29.1%, ($p = 0.132$)). Colonoscopies completed without MEI were associated with higher doses of midazolam ($1.618\,mg \pm 0.051$ vs $1.379\,mg \pm 0.097$, $p < 0.001$), fentanyl ($1.313\,\mu g \pm 0.557$ vs $0.348\,\mu g \pm 0.493$, $p = 0.044$), pethidine ($24.858\,mg \pm 0.986$ vs $23.259\,mg \pm 1.784$, $p = 0.104$) and buscopan ($16.247\,mg \pm 0.526$ vs $13.510\,mg \pm 1.041$, $p < 0.001$). Comfort scores and patient satisfaction outcomes were sub-analysed in colonoscopies completed without analgesia or sedation ($n = 244$). MEI use did not significantly affect endoscopist ($p = 0.383$) or nurse discomfort scores ($p = 0.383$ and $p = 0.971$) or patient satisfaction ratings ($p = 0.209$).
**Conclusion:** Real-world use of MEI at colonoscopy did not improve polyp detection or completion rates but was associated with decreased analgesia, sedation and buscopan use. Unsedated colonoscopy was associated with similar comfort and satisfaction scores regardless of MEI use. Endoscopists may anticipate greater discomfort without MEI and overcompensate sedation doses. Medication dosing should remain consistent regardless of MEI availability.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0712 ASSESSING PREDICTORS OF THE BOWEL PREPARATION QUALITY FOR COLONOSCOPY

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**Introduction:** Colonoscopy is the gold standard for the diagnosis and management of colonic pathology. It is well recognised that the quality of bowel preparation (BP) affects the outcome of colonoscopy. Repeat procedures can be stressful for patients.
The aim from this study is to evaluate factors predicting the quality of BP in a large retrospective cohort.
**Aims & Methods:** All patients undergoing colonoscopy at a tertiary unit between 25th March 2014 and 24th March 2015 were retrospectively identified. The quality indicators used were 'excellent' for no setbacks to mucosal overview. The term 'inadequate' was used to describe suboptimal preparation rendering the procedure unfit for purpose with a requirement for repeat procedure. The term 'adequate' was used to describe stages in between. We investigated the effect of the following factors on the quality of BP:
1. Patient age. 2. Location of BP e.g. inpatient vs outpatient. 3. Number of previous colonoscopies. 4. Referral settings e.g. 2-week wait urgent referrals vs. bowel cancer screening program patients. 5. Pre-assessment and extra counselling. 6. Inflammatory bowel disease (IBD) vs. non IBD indication A logistic proportional odds model was fitted for univariate and multivariate analysis. Data was analysed using R statistical software and the visualizing categorical variables R package.
**Results:** We identified 6467 colonoscopies performed by 72 endoscopists. The patients' median age was 60 (range 7–95). Three hundred and two procedures were performed as inpatient. Twenty percent of the patients were targeted and pre-assessed according to need, 7.5 days before the procedure on average. Almost half the patients were colonoscopy naive. The proportion of excellent, adequate and inadequate procedures was 26%, 63% and 11% respectively. Advancing age ($P < 0.001$), inpatient colonoscopy ($P < 0.001$) and previous colonoscopy experience ($p = 0.02$) were independent predictors of poor bowel preparation. Bowel cancer screening and private patients had significantly better bowel preparation ($P < 0.01$) in comparison to other groups.
**Conclusion:** Bowel preparation is essential to achieve quality in colonoscopy. We identified several independent factors predicting its quality. Older and colonoscopy experienced patients did significantly worse. We suggest focused pre- assessment on those groups. Prospective in-depth studies are required in this field.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0713 THE ADENOMA TO POLYP DETECTION RATE QUOTIENT VARIES AMONG DIFFERENT PATIENT POPULATIONS: IMPLICATIONS FOR THE QUALITY METRICS OF COLONOSCOPY

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**Introduction:** The adenoma detection rate (ADR) is considered the primary quality indicator for colonoscopy and the risk of interval colorectal cancer seems to be inversely related to the endoscopist's ADR. However, ADR calculation is a time-consuming process requiring a combination of endoscopic and histopathological data. The adenoma to polyp detection rate quotient (APDRQ) has been recently proposed as a conversion factor to estimate ADR from polyp detection rate (PDR). Besides issues regarding its calculation, it is still unclear whether different colonoscopy indications may affect its estimation and accuracy.
**Aims & Methods:** Our aim was to calculate conversion factors able to accurately estimate the ADR from the PDR in two different screening populations: average risk patients and patients with a positive fecal immune test (FIT-positive). We retrospectively reviewed colonoscopies carried out by six gastroenterologists from January 2004 to July 2015 in a tertiary referral center for gastrointestinal endoscopy, including only first time colonoscopies on average risk and FIT-positive patients. ADR, PDR and adenoma to polyp detection rate quotient (APDRQ) were calculated for each endoscopist. Mean APDRQs (ADRs/PDRs) for average risk patient population (AVR-APDRQ) and FIT-positive population (FIT-APDRQ) were used as conversion factors to estimate AVR-ADRs and FIT-ADRs of each endoscopist. The main outcome was to measure the strength of the relationship between the estimated and the real ADRs by using Pearson's coefficient, and the average estimated-actual differences.
**Results:** 3686 colonoscopies performed on average-risk patients (2327 female, 63.1%; median age 65, interquartile range 57–72) and 3962 colonoscopies performed on FIT-positive patients (1344 female, 33.9%; median age 63, interquartile range 57–68) were included. The mean AVR-APDRQ and FIT-APDRQ, used as conversion factors, were 0.72 and 0.87, respectively. The correlation between the estimated AVR-ADRs and the actual AVR-ADRs was 0.93 (95% CI, 0.70–1.00; $p = 0.007$), whereas the correlation between the estimated FIT-ADRs and the actual FIT-ADRs was 0.97 (95% CI, 0.83–1.00; $p = 0.002$). Estimated-actual AVR-ADRs difference and estimated-actual FIT-ADRs difference were 0.13% ($SD \pm 1.32$) and 0.02% ($SD \pm 1.32\%$), respectively.
**Conclusion:** In targeted specific populations, the use of a conversion factor applied to the PDR might accurately estimate the ADR. We obtained two targeted conversion factors: 0.72 for average-risk patients, 0.87 for FIT-positive patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0714 CAN A SMALL POLYP SURPRISE A BIG ENDOSCOPIST?

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**Introduction:** Colonoscopy is a significant screening exam for colorectal cancer, providing early detection and potential treatment. The risk of malignancy of large polyps and benign nature of small polyps is generally accepted, however the management of polyps $<10$ mm in diameter including polypectomy technique is controversial and not standardized.

**Aims & Methods:** The aim of the study is to assess the prevalence of malignancy and high grade dysplasia in small 6–9 mm) and diminutive ($<5$ mm) colorectal polyps ($<10$ mm) among patients undergoing screening colonoscopy. We retrospectively analyzed database of 15 631 colonoscopy procedures performed between 2006–2011 in two reference endoscopy centers.

**Results:** The study group included Females = 9476, Males = 6155. The average age of the study group was 54.37 years. In the database there were 4448 patients with polyps found during the procedure and 3943 polypectomy were performed during initial colonoscopy. Among them we found 4245 polyps $<10$ mm in diameter: 3051 (72%) diminutive polyps and 1194 (28%) small polyps. 2 cases of malignancy were discovered in polyps $<5$ mm (0.07%) while malignancy was found in 68 patients with polyps altogether. 26 patients (0.6%) with polyps had high grade dysplasia (most commonly tubular adenoma with HGD), among them 75 cases of HGD were found in small polyps (33 in polyps $<5$ mm (1%) and 42 in polyps 6–9 mm (3.5%).

**Conclusion:** Management of small colorectal polyps is still not standarized and there is no size-based strategy of treatment. Although malignancy is more often found in large polyps, small polyps require attentive approach and adequate removing technique. The cases of high grade dysplasia and malignancy found in polyps smaller than 5 mm can be of great importance to emphasize the necessity to develop a management strategy for small and diminutive polyps.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0715 NEWLY DESIGNED COLONIC EX-VIVO MODEL WITH REAL FLAT LESIONS FOR LEARNING ENDOSCOPIC SUBMUCOSAL DISSECTION IN WESTERN COUNTRIES: DOUBLE EVALUATION INCLUDING EXPERTS' ASSESSMENT AND LEARNING CURVE STUDY ON FELLOWS

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**Introduction:** Endoscopic submucosal dissection (ESD) allows resection of superficial digestive tumors, and is expanding in western countries. However, there is a lack of realistic, available and cost-effective way for learning the technique. We propose a newly designed porcine colonic ex-vivo model, with a two-steps evaluation: one with expert assessment during a single-day workshop, one by a learning curve study with inexperienced fellows

**Aims & Methods:** Model: The model consists of a porcine adult (100 kg) ex-vivo colon and rectum (50 cm). To simulate realistic 0-IIa lesions, we pasted standardized 4 cm patches made of small bowel against the mucosa. Then, the specimen was placed in a specifically designed tray mounted with a hermetic valve mimicking the anus and keeping the air inflation once the scope inserted. Expert's assessment: was performed during a one-day workshop with 21 attendees, whom belonged to the French Group of Practitioners in Endoscopy (GRAPHE), used in advanced endoscopic procedures, including ESDs. Among them, 2 had never performed ESD on patients, 8 had performed less than 10 ESD, 4 between 10 and 30, and 7 more than 30. Thus, 12 considered themselves as "still learning", 9 as "advanced or experts". Six endoscopy stations were available, with various dissection devices. Each attendee evaluated, using a visual analogic scale: 1/ the realism of model itself (8 items); 2/ the realism of the ESD procedure (12 items). Finally, 5 questions were dedicated to their impression about the usefulness of this model for teaching ESD. Learning curve study: 5 fellows without experience in ESD were enrolled and performed 18 procedures each, on 4 cm colonic lesions. For each procedure, it was recorded the time for completing the resection (minutes), the number and the volume on injections (milliliters), the number of position change and of perforations. The first 9 procedures were compared to the last 9 to evaluate the improvement of the skills.

**Results:** Expert's assessment: In total, 42 ESD procedures were performed, with a mean of 2.2 per operator, and the type of knife used was equally distributed. Regarding the evaluation of the model, the results were excellent with rate between 70 and 80% for all the items. More, 100% of the attendees believe that such model is useful to improve skills in ESD and that it could provide them more confidence for patient's procedures, and 100% said that it was an excellent model for learning ESD and were very satisfied by the workshop. More, when comparing the groups of "still learning" and "experts", the mean number of procedures was slightly different (1.8 vs. 2.5, respectively), but there was no difference in the results of the model assessment (20 items as well as final questions). Learning curve study: The total number of procedures was 90. Regarding each operator taken separately, it was observed a significant decreasing of mean ESD time, number of injections and total volume of injections for all of them. There was also less position changes and perforations. The overall analysis (45 first procedures vs 45 last) showed a significant improvement in terms of mean total time ($68 \pm 24$ vs. $41 \pm 13$; $p < 0.001$), number of injections ($4.5 \pm 1.9$ vs. $2.7 \pm 0.8$; $p < 0.001$) and total volume of injection ($69 \pm 26$ vs. $42 \pm 14$; $p < 0.001$). It was also observed a decreasing of perforation rate ($n = 13$ vs. 4; $p = 0.09$).

**Conclusion:** In conclusion, the experts considered this model as excellent for teaching and improving skills, and the learning curve study suggested a significant improvement of the performances with time. This two steps evaluation demonstrated that our newly designed ex-vivo model with simulated realistic lesions was effective and could be a useful model for learning ESD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0716 FACTORS AFFECTING THE IMPLEMENTATION OF NEW ACCEPTED PRACTICES (NAP) TO IMPROVE PATIENTS' SAFETY IN GASTROINTESTINAL ENDOSCOPY UNITS

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**Introduction:** Quality in medicine and patients' safety are major issues in in the last decades and became crucial in all aspects of the health system. In 2013, Gastroenterology units in most Israeli hospitals acquired the approval of the Joint Commission International (JCI) organization following prolonged procedure of training and qualification.

**Aims & Methods:** To assess the factors affecting the successful implementation of NAP aimed at improving patients' safety in endoscopy units in 3 JCI- qualified hospitals in central Israel. We used questionnaires and statistically analyzed the data using t-test and Pearson Correlation Coefficient Calculator. We investigated the followings: 1) the association between knowledge and positive attitude of the endoscopy stuff to the NAP regarding hands hygiene, performance of time out before endoscopy and double check of pathology specimens, 2) factors that inhibit or assist in the implementation of the NAP, 3) the differences in performance level parameters of the NAP between physicians and nurses in the endoscopy units.

**Results:** 71 endoscopy units personal participated in the study (64% females and 36% male, 49% nurses and 51% physicians, mean age was $45.7 \pm 9.4$ years). We found no positive correlation between the level of knowledge of each of the NAP (hands hygiene, time out and pathology specimen handling) to their actual implementation, but there was a significant correlation between positive attitude to the NAP and the level of actually performing them. The NAP performance by GI nurses was higher compared to the physicians concerning time out and pathology specimens handling. The major factors that prohibited the implementation of the NAP were former organization habits and work stress. According to the questionnaires, the means to improve implementation of the NAP should be: discussions in stuff meetings of the endoscopy unit, group decision making and consent of the stuff to comment to each other when necessary.

**Conclusion:** Knowledge and positive attitude are not sufficient for successful implementation of NAP in GI endoscopy units. In order to achieve a major change in adopting the new practices we need to abandon former organization habits, to include the stuff in the process of implementation and to reduce work stress by improving time management.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0717 HIGHER NUMBER OF SMALL (<10MM) ADENOMAS DETECTED WITH ENDOCUFF-ASSISTED COLONOSCOPY IN A SCREENING POPULATION

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**Introduction:** The Adenoma Detection Rate (ADR) is one of the quality measures in screening colonoscopy. The lower the ADR, the higher the risk of cancers after colonoscopy. Moreover, the number of adenoma detected per patient could impact on surveillance. Endocuff is an endoscopic cap with plastic projections which permits to flatten the colonic fold during withdrawal. Endocuff-Assisted colonoscopy (EAC) is potentially able to ameliorate the ADR which is crucial especially in a screening population.
**Aims & Methods:** To compare in a screening population ADR, advanced adenoma detection rate (AADR) and mean number of adenomas per patient (MAP) between EAC and Standard colonoscopy (SC)**.** We compared the performance of SC (from January to December 2014) and EAC (from January to December 2015) both in consecutive Fecal Immunochemical Test (FIT) positive and endoscopical follow-up screening participants. Colonoscopy was performed by the same team of endoscopists in both 2014 and 2015. ADR was defined as the number of colonoscopy with at least one adenoma divided by the total number of colonoscopies; mean number of adenoma per patient was defined as the total number of detected adenomas divided by the number of colonoscopies; AADR as the number of colonoscopy with at least one advanced adenoma (defined as an adenoma of 1 cm or grater, or with villous/tubule-villous or components or with high grade dysplasia) divided by the number of colonoscopies.
**Results:** 579 (298 M, mean age: 60 years, 49–70) and 605 (343 M, 60 ys, 49–70) subjects performed SC and EAC respectively. ADR was 48% in SC and 53% in EAC, p = ns. MAP in SC and EAC was 0.88 (range: 0–8) and 1.1 (range: 0–13) respectively, p = 0.02. Advanced adenoma detection rate was 26% and 23% in SC and EAC respectively, p = ns.
**Conclusion:** EAC increases the number of small (< 10 mm) adenomas detected (but not both ADR and AADR) shortening surveillance intervals in accordance to the current guidelines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0718 PREVALENCE OF SERRATED ADENOMAS/POLYPS AT COLONOSCOPY IN A REGIONAL HOSPITAL IN QUEENSLAND, AUSTRALIA

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**Introduction:** Serrated adenomas or polyps (SSA/P) of the colo-rectum are established precursors of colorectal cancer. Cancers associated with SSA/Ps are often in the proximal colon. These polyps are often flat and barely discernible and account for a significant fraction of post colonoscopy interval cancers. While recent publications suggest that SSA/Ps are more common than previously realised, data on the prevalence of these polyps is limited. Most of the published literature in this area has measured prevalence rates in screening populations and in tertiary centres.
**Aims & Methods:** The aims of our study were 1) to establish the prevalence of SSA/Ps at colonoscopy in a regional centre in South East Queensland 2) To identify the prevalence of SSAs in the younger population ie <40 years. Data was collected from our endoscopy database between July 2014 and December 2015. All procedures performed by Gastroenterologists and Surgeons who performed more than 100 colonoscopies annually were used for the analysis. Histopathology was used for establishing presence of serrated lesions and size. Electronic records stored were interrogated to establish age and gender of the patient and location of the lesion. Prevalence was determined as the proportion of patients with at least one serrated adenoma/polyp.
**Results:** A total of 3173 procedures were identified and were performed by 13 endoscopists (8 physicians, 5 surgeons). 460 SSA/Ps were detected in 309 examinations with a prevalence of 9.7%. 194 patients had polyps in the proximal colon only(62.8%). 82 polyps were greater than 10 mm in size with 85% of them in the proximal colon. Similarly, of all SSA/Ps discovered, 323 (70%) were in the proximal colon. 52.4% of the serrated polyps were discovered in men and 47.6% in women. Analysis of prevalence of SSA/Ps in relation to age was performed and identified that 10.4% of the procedures that detected SSA/Ps were in the under 40 years population. The prevalence of SSA/Ps in this age group was 1%. Details of the distribution across the age groups is provided in the attached table.

| Age Group | Procedures with SSA | Percentage | Prevalence |
|---|---|---|---|
| 20–39 years | 32 | 10.4% | 1% |
| 40–59 years | 118 | 38.2% | 3.7% |
| 60–79 years | 150 | 48.5% | 4.7% |
| 80–100 years | 9 | 2.9% | 0.2% |

**Conclusion:** Serrated adenomas/polyps are more common than realised in our population. In a retrospective analysis of a large number of unselected procedures we identified a prevalence of SSA/Ps of 9.7%. We also identified a significant proportion of procedures for patients less than 40 years where these polyps were discovered. Improvements in image enhancement and quality in colonoscopy with a focus on adenoma detection and withdrawal times may further increase serrated adenoma detection. This is expected to have a positive impact on reducing proximal colon cancers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0719 HISTOLOGY PREDICTION OF COLORECTAL POLYPS BY NARROW-BAND IMAGING – ACCURACY AND INTER-OBSERVER AGREEMENT IN STATIC IMAGES' EVALUATION

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**Introduction:** The characterization of colorectal polyps by Narrow-band imaging (NBI), using the NICE classification (NBI-International Colorectal Endoscopic Classification), recently complemented by the WASP classification (Workgroup Serrated Polyps and Polyposis) revealed high accuracy when applied by endoscopists with experience in electronic chromoendoscopy. It remains to determine its applicability beyond the scope of clinical trials.
**Aims & Methods:** To assess the accuracy and inter-observer agreement of the NICE/WASP classifications for predicting the histology of colorectal polyps. NBI photo documentation of polyps detected during colonoscopy (colonoscopes CF-H190®, Olympus, Europe), from January-February 2016. High-quality images selected (Visual Analogue Scale > 6) and reviewed by 8 gastroenterologists and 4 residents, with no previous NBI experience, except for a 20-minutes interactive session. Polyps' images classified as hyperplastic polyp (1p), serrated (1s) or adenoma (2) (NICE/WASP classifications) and a confidence level was assigned to the predictions (low: <90% vs high: >90%). Individual performance, global and inter-observer agreement was evaluated. Statistics: logistic regression, Fleiss Kappa (SPSS-21).
**Results:** 52 images were evaluated, corresponding to 16 hyperplastic polyps (30.8%), 4 serreated (7.7%) and 32 adenomas (61.5%). The adenomatous histology prediction of NICE/WASP classifications revealed an overall accuracy, sensitivity, specificity, positive predictive value and negative predictive value of 80.9%, 95.4%, 71.9%, 96.2% and 68.0%, respectively. Individual accuracy ranged from 63.5% to 92.3%. 70.5% (440/624) of ratings were assigned with a high confidence level. Inter-observer agreement was moderate (Fleiss Kappa 0.53; 95% CI, 0.44–0.62), with no significant difference between specialists (Fleiss Kappa 0.51; 95% CI, 0.42–0.61) and residents (Fleiss Kappa 0.58; 95% CI, 0.49–0.67).
**Conclusion:** The application of the NICE/WASP classifications by endoscopists with no NBI experience showed good accuracy, in spite of high variability and moderate inter-observer agreement. The limitations associated to the use of static images without magnification may have contributed to these results.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0720 COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN WESTERN WORLD: PROMISING LESSONS FROM A PROSPECTIVE SERIES OF 85 CASES

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**Introduction:** Endoscopic submucosal dissection (ESD) has been proposed as an ideal technique for early colorectal neoplasms that are large and/or with suspected submucosal fibrosis/focal adenocarcinoma. A demanding learning curve for colorectal ESD, together with a low prevalence of easier gastric or esophageal lesions to boost it, have prevented colorectal ESD spreading in Western countries.

**Aims & Methods:** To evaluate outcomes and learning curve progress of colorectal ESD, we completed a prospective analysis of procedures performed in two tertiary centers in Madrid. Previous training included intensive practice in animal model (46 colorectal ESD and a short number of gastric ESD performed without tutoring). We performed a global analysis and also time-framed analysis of the series, specifically assessing initial success, en-bloc & R0 resection rate, speed and complication rate. Perforation was established as any disruption of the muscular layer, regardless of size or identification of peritoneal fat.

**Results:** ESD was attempted in 85 colorectal lesions by a single operator (AH) from November 2012 to April 2016. Rectal lesions comprised 22.4% of the total collection analysed. Anatomical distribution of colonic lesions were as follows: cecum (9, 16.5%), ascending colon (9, 10.6%), hepatic flexure (8, 9.4%), transverse colon (14, 16.5%), splenic flexure (4, 4.7%), descending colon (7, 8.2%), sigmoid colon (9, 10.6%) and colorectal anastomosis (1, 1.2%). Classification according to morphology was: LST Granular mixed type 8 cases (12.1%), LST Granular homogeneus type 36 cases(54.5%) and LST Non Granular type 22 cases (33.3%). Initial success was achieved in 95.3% of the cases, with en-bloc and R0 resection rate of 94.1% and 85.8% respectively. Mean lesion size was 31 mm (range 5–80 mm), with median time to complete procedure 85 min (range 23–260 min). Perforation was the predominant complication, with a global rate of 38.8%. Close to 85% of the perforations were successfully managed endoscopically. Results from the learning curve progression according to 3 consecutive chronological blocs of 25 cases and a last bloc of 10 cases are summarized in table 1. Initial success rapidly increased from 84% to 100%, whereas en-bloc resection rate remained very high from the beginning. Speed of ESD showed a constant advance after the first 50 cases (from 0.16–0.17 $cm^2$/min on the first 50 cases to 0.33 $cm^2$/min on the last 10 cases). Perforation rate remained constantly high along all the learning curve (36–40%). Of note, surgical treatment was required on average 20% of the perforations along the first 50 cases, but a decrease in the following 2 periods analysed (11% and 0%) was remarkable.

| N = 85 | 1–25 | 26–50 | 51–75 | 76–85 | Total(n/%) |
|---|---|---|---|---|---|
| Success | 21(84%) | 25 (100%) | 25 (100%) | 10(100%) | 81(95.3%) |
| En bloc (n/%) | 21(100%) | 24(96%) | 25 (100%) | 10(100%) | 80(94.1%) |
| R0 (n/%) | 21 (100%) | 23 (92%) | 20 (80%) | 9(90%) | 73(85.8%) |
| Speed ($cm^2$/min) Mean (SD) | 0.17(0.13) | 0.16(0.12) | 0.22(0.17) | 0.33(0.15) | 0.21(0.15) |
| Perforation (n/%) | 10 (40%) | 10 (40%) | 9 (36%) | 4 (40%) | 33(38.8%) |
| Surgery after perforation (n/%) | 2/10(20%) | 2/10(20%) | 1/9(11.1%) | 0/10 (0%) | 5 (15.2%) |

**Conclusion:** Colorectal ESD is a demanding technique with a long learning curve in Western setting, as reflected in a high perforation rate observed along the time. Nevertheless, excellent outcomes in terms of success, en-bloc resection rate, speed and endoscopic management of perforations can be accomplished after completing 50 cases. These preliminary results require further analysis with long-term recurrence rate to properly evaluate the real impact of colorectal ESD in the West.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0721 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASMS MORE THAN 50MM IS A FEASIBLE METHOD OF TREATMENT

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**Introduction:** Endoscopic submucosal dissection for colorectal neoplasms (C-ESD) has become a standard method of treatment. One of the advantages of ESD is that it makes it possible to resect a large tumor in an en block fashion, but a previous report [1] revealed that C-ESD for large lesions ≥50 mm was an independent risk factor for complications.

**Aims & Methods:** In the present study we aimed to evaluate the safety of C-ESD for the lesions ≥ 50 mm. This is a retrospective single-center analysis. We extracted all consecutive C-ESD cases between January 2010 and January 2016 from our database. Out of the extracted cases, we excluded aborted cases and cases where the histopathological result proved to be non-neoplastic or advanced cancer. We divided the remaining cases into two groups: the diameter of the tumor was (A) between 20 mm and 49 mm; (B) ≥ 50 mm. The following factors were assessed and compared between the two groups: patient characteristics, tumor shape, tumor location, pathological results, procedure time, and complications.

**Results:** A total of 327 cases were enrolled in this study. The results were shown in Table 1. Group A contained 285 cases (mean age: 66.9 ± 11.3, male 187/female 98) and group B contained 42 cases (mean age: 64.8 ± 10.5, male 22/female 20). As for macroscopic type, significantly more cases of laterally spreading tumor-granular type (LST-G) were included in group B than A, and no protruded tumors were included in group B ($P < 0.001$). The mean resected tumor diameter were 31.0 ± 8.0 mm in group A and 67.3 ± 15.7 mm in group B. The procedure time was significantly longer in group B than in group A (90.7 ± 52.9 min in group A vs 163.2 ± 76.5 min in group B). En block resection was achieved in 276 cases (96.8%) in group A and 42 (100%) in group B, respectively, but curative resection cases (A: 221, 76.5%; B: 23, 54.8%) were significantly more in group (A). Of the 19 non-curative cases in group B, 18 cases were with horizontal margin positive or unknown, and to date no recurrence has occurred for these cases. As for complications, there were no significant differences in the rate of post-ESD bleeding, perforation and delayed perforation between group A and B (post-ESD bleeding/perforation/delayed perforation: 2.1%/2.8%/0.7% in group A vs 4.8%/4.8%/2.4% in group B).

**Table 1:** The characteristics of patients and tumors, and the resection results

| | Group (A) 20–49 mm | Group (B) ≥ 50 mm | P value |
|---|---|---|---|
| Case number | 285 | 42 | |
| Age, y | 66.9 ± 11.3 | 64.8 ± 10.5 | 0.264 |
| Sex (female/male) | 98/187 | 20/22 | 0.101 |
| Macroscopic type, n (%) | | | < 0.001 |
| LSTG | 118 (41.4) | 38 (90.5) | |
| LSTNG | 131 (46.0) | 4 (9.5) | |
| protruded | 36 (12.6) | 0 (0) | |
| Location, n (%) | | | 0.099 |
| proximal | 143 (50.2) | 16 (38.1) | |
| Distal | 67 (23.5) | 8 (19.1) | |
| Rectum | 75 (26.3) | 18 (42.9) | |
| Tumor diameter, mm | 31.0 ± 8.0 | 67.3 ± 15.7 | |
| Resected specimen diameter, mm | 37.8 ± 8.9 | 72.5 ± 16.9 | |
| Histopathological findings, n (%) | | | 0.001 |
| adenoma | 137 (48.1) | 13 (31.0) | |
| pTis (intramucosal carcinoma) | 101 (35.4) | 28 (66.7) | |
| pT1a (submucosal invasion ≤1000$\mu$m) | 27 (9.5) | 0 (0) | |
| pT1b (submucosal invasion >1000$\mu$m) | 20 (7.0) | 1 (2.4) | |
| Procedure time, min | 90.7 ± 52.9 | 163.2 ± 76.5 | < 0.001 |
| En block resection, n (%) | 276 (96.8) | 42 (100) | 0.611 |
| Curative resection, n (%) | 221 (76.5) | 23 (54.8) | 0.003 |
| Post-ESD bleeding, n (%) | 6 (2.1) | 2 (4.8) | 0.274 |
| Perforation, n (%) | 8 (2.8) | 2 (4.8) | 0.623 |
| Delayed perforation, n (%) | 2 (0.7) | 1 (2.4) | 0.339 |

**Conclusion:** C-ESD for the lesions ≥ 50 mm takes a longer procedure time, but can be performed safely. Almost all of the non-curative cases in group B in this study were caused by lateral positive margin, so there is room for improvement. C-ESD for the lesions ≥ 50 mm can be safely said to be feasible and safe.

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### P0722 IDENTIFICATION AND QUANTIFICATION OF THE CLINICAL FEATURES OF INFLAMMATORY BOWEL DISEASE AND COLORECTAL CANCER IN PATIENTS AGED <50 YEARS: WHO NEEDS URGENT COLONOSCOPY

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**Introduction:** In younger patients (aged <50 yrs) colorectal cancer (CRC) and inflammatory bowel disease (IBD) can present with similar symptoms and both are often diagnosed after significant delay. Clinical decision tools that quantify risk of disease by symptoms, individually or in combination, are increasingly used by clinicians. One possible way of achieving earlier diagnosis of IBD and CRC is to consider which patients aged <50 yrs need specialist assessment for possible serious bowel disease. We identified and quantified features of CRC and IBD in primary care, separately and combined.
**Aims & Methods:** This was a case–control study using electronic primary-care records of UK patients aged <50 years. Cases with primary colorectal cancer or IBD were matched to controls on age, sex and practice. Putative features were identified in the year before diagnosis. Odds ratios (ORs) were calculated for these features using conditional logistic regression, and positive predictive values (PPVs) were calculated.
**Results:** A total of 11239 cases and 26926 controls were studied. Ten features were independently associated with CRC/IBD (all $P < 0.001$): abdominal pain, OR 3.9 (95% confidence interval 3.4–4.5); change in bowel habit, 27.0 (19.0–39.0); diarrhoea, 8.9 (7.5–11.0); rectal bleeding, 42.0 (33.0–55.0); low haemoglobin, 2.5 (2.1–3.1); low MCV, 2.7 (2.1–3.5); raised inflammatory markers, 5.4 (4.6–6.3); raised hepatic enzymes, 1.4 (1.2–1.6); raised white cell count, 1.5 (1.3–1.9); and thrombocytosis, 4.4 (3.4–5.7). PPVs >5% in patients <50 years were found for rectal bleeding in combination with thrombocytosis or raised inflammatory markers, for change in bowel habit with low MCV or low haemoglobin, and for diarrhoea in combination with thrombocytosis.
**Conclusion:** Symptoms of colorectal cancer and inflammatory bowel disease are similar in younger patients presenting in primary care. When associated with abnormal haematology, rectal bleeding and change in bowel habit are strongly predictive of CRC/IBD and can be used to prioritise patients for colonoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0723 NARROW BAND IMAGING (NBI) VS. NBI WITH ACETIC ACID ENHANCEMENT FOR DIFFERENTIATION OF SMALL COLORECTAL POLYPS

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**Introduction:** Narrow Band Imaging Endoscopy (NBI) is useful for differentiation of adenomas and hyperplasic polyps (HP). However, it is still occasionally complicated for distinguishing polyps using just a NBI, because it's surface is often indistinct. The application of acetic acid for enhancement allows obtain a clearer image.
**Aims & Methods:** To evaluate the diagnostic efficacy NBI and NBI with acetic acid enhancement (NBI+AA) for differentiation of adenomas and HP. We carried out a prospective study that included 261 benign colorectal polyps with size less than 10 mm (the average size of polyp was 4.8 mm). All polyps were detected by the conventional inspection in white light mode. Afterwards 184 polyps have been examined with NBI mode, however 35 polyps (23.5%) were excluded due to the fact that lesions surface was unclean and unsuitable for evaluation by NICE-classification. Ultimately in NBI-group entered 149 cases. In NBI+AA-group 77 polyps were included, all of them were evaluated after the utilization of1.5% acetic acid spray. Eventually 226 cases were involved into the study (73 adenoma and 153 HP). Endoscopy suites were equipped with Evis Exera II CV-180 processors, CF-H180AL and PCF-H180AL colonoscopes (Olympus). In each case the image database has been generated in graphical format.bmp. After completing inclusion of patients in the study, physician, who conducted a colonoscopy, predicts the results of histological findings based on the NICE classification.
**Results:** In both groups (NBI-group vs. NBI+AA-group) the sensitivity of endoscopic prediction compose 84.6vs.92.7% (CI 84.7–97.3% for NBI+AA-group), the specificity 99.1vs.98.6% (CI 92.5–99.7%), the positive predictive value 99.3vs.98.7% (CI 92.9–99.8%), the negative predictive value 81.9vs.92.2% (CI 83.8–99.1%) and AUC 0.92vs.0.96% (CI 91–98%). In NBI-group relative risk was 0.82 ($P < 0.0001$), odds ratio was 0.031 ($P < 0.0007$), in NBI+AA-group 0.93 ($P = 0.05$) and 0.16 ($P = 0.088$) respectively.
**Conclusion:** Both of these methods (NBI and NBI+AA) are highly accurate for distinguishing adenomas and HP of small size. Nevertheless, applying NBI-mode is limited in approximately a quarter of the cases (23.5%) due to indistinct surface of lesions. Acetic acid enhancement increases the value of this method. Usage of acetic acid is cheap, fast, safe and allows avoiding unnecessary biopsies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0724 ENDOSCOPIC APPLICATION OF REGENERATED OXIDIZED CELLULOSE AFTER RECTAL ENDOSCOPIC RESECTION

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**Introduction:** The most common complication of endoscopic resection (ER) of large colorectal polyps is bleeding, especially in patients who must continue anticoagulation medications for thrombophilic or cardiovascular disorders. Oxidized cellulose mesh (Surgicell®) is a well-known and widely available surgical hemostatic agent (mesh). Oxidized cellulose, which has bactericidal activity, exerts its effect as a tissue-apposing device. Oxidized cellulose is used to stop bleeding from liver lacerations, gynecological surgery and in neurosurgical interventions. Therefore, it use in endoluminal GI interventions is appealing, especially in patients on anticoagulant therapy.
**Aims & Methods:** The aim of this study was to evaluate the feasibility of endoscopic application of oxidiced cellulose and the hemostatic efficacy after endoscopic resection (endoscopic submucosal dissection or piecemeal endoscopic mucosal resection). Retrospective, observational, open label, single-center study of patients undergoing endoscopic resection of large rectal and rectosigmoid lesions. After the colorectal epithelial neoplasm removed, oxidized cellulose was applied onto the submucosal surface using one of two methods: a) anoscope or cap-assisted delivery. In both techniques, a hemoclip was advanced through the working channel of the scope and 10 x 10 to 20 x 20 mm large pieces of the oxidized cellulose were grasped with the clip and then delivered and attached to the wound.
**Results:** A total of 16 patients (9 male, 7 female, mean age 65, range 42 to 87) underwent endoscopic resection (ESD, n = 9 or piecemeal EMR, n = 7) of large rectum or rectosigmoid lesions with either primary intent of complete resection or debulking (in the case of large mucin-secreting rectal tumors). All patients were on anticoagulants and/or antiplatelet agents. The mean size of the lesions was 45 mm, range 30 to 120 mm. An endoscopic R0 was achieved in 75%. During follow-up period there were no rectal bleeding episodes or adverse events, despite patients continuing on anticoagulant therapy.
**Conclusion:** Oxidized cellulose mesh can be successfully applied to large resection sites using the cap-assisted or anoscope techniques. Oxidized cellulose mesh effectively decreases hemorrhage and prevents post-endoscopic resection bleeding. Thus, this feasibility study suggests that oxidized cellulose mesh may be a valuable tool to provide hemostasis and prevent bleeding after ESD. Now prospective and randomized studies are warranted.
**Disclosure of Interest:** K. Mönkemüller: Honoraria for lectures/teaching: Cook Medical USA, Ovesco Tuebingen, Germany
All other authors have declared no conflicts of interest.

### P0725 THE EFFICACY AND SAFETY OF ENDOSCOPIC MUCOSAL RESECTION USING BIPOLAR INSTRUMENT IN LARGE PEDUNCULATED COLORECTAL POLYPS

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**Introduction:** Background: It is known that pedunculated colorectal polyps are high risk for post-polypectomy bleeding (PPB), because thick feeding artery runs through their stalks[1]. Therefore, several methods for endoscopic treatment, such as endoloop snare and clips to the stalk, have been performed to prevent PPB in large pedunculated polyps. However, it is relatively difficult for endoscopists and assistants to perform using these methods because of technical tools and limited endoscopic working space. Moreover, if spurting bleeding after polypectomy occurred, it was difficult and time consuming to do hemostasis because of poor visibility due to bleeding. In our hospital, large pedunculated polyps are removed with endoscopic mucosal resection (EMR) method by bipolar electrocauterization. In this method, several benefits are present. The precoagulation with slowly cutting because of electric current flow peculiar to bipolar snare that does not flow through the wall of colon can prevent immediate PPB. Furthermore, if immediate PPB occurred, hemostasis was relatively easy with bipolar hemostatic forceps, because we could observe the bleeding point by large resection space after EMR. Therefore, we consider EMR by

bipolar electrocauterization is a good method for large pedunculated polyps in the respect of a lesser PPB and easier hemostasis. In previous studies, PPB accounted for 5.1–14.4% by monopolar electrocauterization and 1.8–3.1% by bipolar electrocauterization with some preventional methods[2–4].
**Aims & Methods:** The aim of this retrospective study is to investigate the efficacy and safety of removal of large pedunculated colorectal polyps with EMR by bipolar electrocauterization. Methods: We intended consecutive patients with pedunculated colorectal polyps 10 mm or more that were resected with EMR by bipolar electrocauterization in our hospital between May 2013 and October 2015. The data about patients' characteristics and endoscopic findings were evaluable retrospectively. We assessed about PPB and prophylactic hemostasis in pedunculated polyps resected with EMR.
**Results:** A total of 50 polyps in 39 patients were analyzed. The median head and stalk diameter were 15 mm (range, 10–40) and 10 mm (range, 6–20), respectively. The location of polyps was almost in Sigmoid colon. Prophylactic clips before and after EMR were performed at 0 and 1 polyp in all polyps. PPB was observed 5 polyps (10%) in 4 patients, compromised of 3 immediate PPB (6%) in 3 patients and 2 delayed PPB (4%) in 1 patient. The hemostasis of post EMR performed in 37 polyps (74%) by hemostatic forceps and no PPB observed in those polyps.
**Conclusion:** This was the first report about removal of pedunculated polyps with EMR method by bipolar electrocauterization. This method was tolerable safety and efficacy compared with previous studies, and could be one of the choices to remove large pedunculated polyps.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0726 ENDOSCOPIC RESECTIONS BY EMR AND ESD IN CIRRHOTIC PATIENTS: A SAFE AND EFFICIENT PROCEDURE?


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**Introduction:** Endoscopic resection of intra mucosal carcinomas or precancerous lesions is established as a safe method to achieve a high rate of R0 curative resections. However, it has not been shown whether cirrhotic patients could safely benefit from this procedure. Intra-abdominal surgery is a high-morbidity and high-mortality procedure in cirrhotic patients, the main risk being hepatic decompensation. Endoscopic resection could be an interesting alternative to reduce such risks. On the other hand, portal hypertension, especially in esophagus, stomach or rectum can be an impediment to resections, as the submucosal venous dilations easily bleed. Endoscopists and anaesthetists are also precautious regarding clotting factors ant platelets abnormalities. The aim of our study was to assess the safety and effectiveness of endoscopic resections in this case.
**Aims & Methods:** We designed a retrospective, open-label monocenter study. Every patient diagnosed cirrhotic, either through medical imaging, liver biopsy or Transient Elastometry along with physical examination and blood results, admitted in our unit for an endoscopic resection (Endoscopic Submucosal Dissection (ESD) or Endoscopic Mucosal Resection (EMR)) or a Per Oral Endoscopic Myotomy (POEM) between 2009 and 2016, was included. Data on patients' medical history, cirrhosis, blood results, endoscopic procedure, and potential complications were retrieved from medical records. Medical records were fully screened for any clue of retarded complication that would not have been mentioned in the post procedure report. Last medical note was considered end of follow up.
**Results:** To date, 102 resections were included from medical procedures coding records. After medical records analysis, 88 fitted our criteria (cirrhosis + ESD, or EMR, or POEM), in 52 patients (Esophagus n = 32, Stomach n = 25, Duodenum n = 15, Colon n = 14, POEM n = 2). Patient globally had a mild liver disease: the mean MELD score was 9.15. Only 10 patients had a decompensated cirrhosis (defined by ascites presence). Out of the 35 with precise available data, 19 had a history of hepatic decompensation. 36 patients had a history of varices band ligation (no band ligation n = 16, missing data n = 36). The mean follow up duration after resection was 17.35 months (from 0.03 to 52.20). 22 resections were performed in patients with antiplatelet medication. 3 patients had a creatinine clearance below 30 mL/min, 13 between 30 and 60 mL/min, 33 between 60 and 90 mL/min, and 41 over 90 mL/min. There were no cirrhosis decompensation, nor post-endoscopic infections in all 88 cases (0%). 8 bleedings, in 6 different patients occurred: in the Stomach n = 1 (4%), the Duodenum n = 3 (20%) and the Colon n = 4 (28.6%). The overall bleeding rate was 9.1%. The mean MELD score in patients who bled was 10.1 (vs 9.1 in patients who did not bleed), none had a decompensated cirrhosis. All bleedings happened within 48 hours of the procedure, and either spontaneously dried up (n = 5) or were successfully treated in endoscopy (n = 3). 5/8 were carried out in patients with antiplatelet medication (62.5%). The bleeding rate in cirrhotic patient under antiplatelet medication in the overall cohort was 22.7%. Creatinine mean was 110.8 μmol/L and creatinine clearance mean was 66.5 mL/min (vs respectively 83.6 μmol/L and 92.9 mL/min in patients who did not bleed). Among patients who experienced delayed bleeding, 6 had stage III chronic kidney failure (clearance of creatinine between 30 and 60 mL/mn). The bleeding rate in patients with a creatinine clearance below 60 mL/min in the overall cohort (stage III to V chronic kidney disease) was 31.6%. There were no bleeding-associated deaths. No other complication was observed.

| Total: 88 resections | Bleeding (8) | No bleeding (80) |
|---|---|---|
| **Mean Age (year)** | 62.38 | 66.4 |
| **Gender Men** | 6 (75%) | 73 (91.25%) |
| **Women** | 2 (25%) | 7 (8.75%) |
| **Localisation Œsophagus** | 0 (0%) | 32 (40%) |
| **Stomach** | 1 (12.5%) | 24 (30%) |
| **Duodenum** | 3 (37.5%) | 12 (15%) |
| **Colon** | 4 (50%) | 10 (12.5%) |
| **POEM** | 0 (0%) | 2 (2.5%) |
| **Mean Large Diameter (mm)** | 11.83 | 19.6 |
| **Medication antiplatelets** | 5 (62.5%) | 15 (19%) |
| **K vitamin inhibitors** | 0 | 2 (2.5%) |
| **both** | 0 | 4 (5.1%) |
| **Mean Hospital stay (days)** | 4.9 | 4.5 |
| **Mean Hemoglobin drop (g/dL)** | 0.6 | 0.21 |
| **Mean Albumin (g/L)** | 39.2 | 36.8 |
| **Mean Bilirubin (μmol/L)** | 8.3 | 13.6 |
| **Mean Platelets Count (G/L)** | 171 | 166 |
| **Mean INR** | 1.08 | 1.13 |
| **Mean Creatinin (μmol/L)** | 110.8 | 83.6 |
| **Mean Clearance (μmol/mn)** | 66.5 | 92.9 |
| **Mean PT** | 91 | 83.3 |
| **Mean MELD** | 10.1 | 9.1 |
| **CHILD-PUGHA5-A6-B7** | 8 (100%) | 73 (91.25%) |
| **>B8** | 0 (0%) | 7 (8.75%) |
| **Mean Follow up (months)** | 13.22 | 17.78 |
| **Death** | 0 (0%) | (7.6%) (4 patients) |

**Conclusion:** Endoscopic resection does not seem to induce cirrhosis decompensations unlike open abdominal surgery. Our results tend to demonstrate that endoscopic resections are safe and effective in cirrhotic patients. The risk of delayed bleeding is increased in case of association of both cirrhosis and antiplatelet agents with 5 bleedings among the 88 resections.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0727 RISK ASSESSMENT OF ANTICOAGULATION AND ANTIPLATELET THERAPY IN DELAYED POSTPOLYPECTOMY BLEEDING – A COHORT STUDY


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**Introduction:** Colonic polypectomy of adenomatous polyps reduces the incidence and mortality from colorectal cancer. However it can be associated with potentially serious complications, such as delayed bleeding.
**Aims & Methods:** The aim of this study was to assess the risk of delayed postpolypectomy bleeding in patients receiving anticoagulation (AC) and/or antiplatelet (AP) therapy. Retrospective cohort study of patients who underwent colonic polypectomy between January and December 2015 after discontinuation of AC and/or AP according to current recommendations. Data collected included patient demographics and antithrombotic therapy, endoscopic technique, lesion characteristics and bleeding incidence.
**Results:** We analysed 913 patients, 63% were women with a mean age of 66.9 ± 10.7 years. Fifty-nine patients were under anticoagulation, 166 were on antiplatelet agents and 5 under dual antithrombotic therapy (AC and AP). Overall 2321 lesions were resected, with a median of 2 (1–18) lesions per patient. The resected lesions had more than 10 mm in 380 cases and 429 patients had lesions located in the right colon. Delayed post-polypectomy bleeding occurred in 11 patients (1.2%), all managed successfully with endoscopy, without need of surgery and without bleeding-related death. The incidence of delayed bleeding

was 0.3% (2/683) in patients without antithrombotic therapy, 1.2% (2/166) in patients receiving AP, 6.8% (4/59) in patients under AC and 60% (3/5) in patients with dual antithrombotic therapy. The risk of delayed bleeding was significantly increased with AC (OR 24,764; 95% CI 4,4437–138,220; $P < 0.001$) and dual antithrombotic therapy (OR 510,75; 95% CI 53.06–4916.23; $P < 0.001$). There was no difference in bleeding risk between patients under antiplatelet drugs and without medication (OR 4,152; 95% CI 0.58–29.70; $P = 0.156$). The incidence of delayed bleeding was similar in patients under warfarine and new oral anticoagulation therapy.
**Conclusion:** The incidence of post-polypectomy delayed bleeding was higher in patients receiving anticoagulant agents. These findings suggest the need of a close surveillance after polypectomy/mucosectomy in these patients, even after a proper interruption of therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0728 PREDICTING ADENOMA DETECTION RATE BY POLYP DETECTION RATE AND INDIVIDUAL ADENOMA-TO-POLYP-DETECTION-RATE-RATIO IN AVERAGE-RISK COLONOSCOPIES

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**Introduction:** Adenoma detection rate (ADR) has been established as a quality indicator for screening colonoscopy.[1] However, it is cumbersome to obtain in routine practice. The adenoma-to-polyp–detection-rate-ratio (APDRR) has been proposed as a practical tool to easily estimate the ADR in routine practice.[2,3]
**Aims & Methods:** The aim of this study was to evaluate the APDRR in order to estimate ADR. We performed a retrospective evaluation of average risk screening and surveillance colonoscopies in a community and tertiary academic hospital setting. Individuals with an increased risk for colorectal cancer, with proven polyps who have been referred for polypectomy, and with a sigmoidoscopy only were excluded. Polyp detection rate (PDR), ADR and APDRR were calculated as previously described.[3] APDRR was either calculated as group average for all endoscopists and the first half of study procedures or individually for each endoscopist and his/her first 25, 50, and 100 colonoscopies. Estimated ADR (ADR_est) was calculated as the product of endoscopist's PDR and either the averaged group APDRR for the second half of study procedures or the individual APDRR of his/her first 25, 50, and 100 colonoscopies for his/her subsequent procedures grouped in portions of 50 procedures. We used Pearson's correlation coefficient (r) to describe the strength of association between ADR and ADR_est. Wilcoxon matched-pair signed-rank was used to test the difference between different prediction models. The root-mean-square error (RMSE) was defined as $\sqrt{(\text{ADR-ADR\_est})^2}$. A p-value $<0.05$ was considered statistically significant.
**Results:** A total of 2,717 patients were analyzed. 45.7% were men, the median age was 61.8 years (interquartile rage 56.2, 68.7). Overall PDR and ADR were 52.6% and 35.1%. The averaged group APDRR for the entire study period was 0.667. RSME between ADR and ADR_est was 5.8% with no significant correlation between both parameters ($r = 0.189$, $p = 0.684$) when the averaged group APDRR was used. In the individual approach using the first 50 colonoscopies to calculate APDRR, ADR and ADR_est correlated significantly in 4 of 5 endoscopists with a mean RMSE of 6.8% (2 of 5 and 3 of 5 endoscopists with mean RMSE of 9.9% and 5.8% using first 25 and 100 colonoscopies as basis for APDRR, respectively). A significant difference in mean RMSE was found in the Wilcoxon matched-pair signed-rank for the prediction model 25 and 50 ($p < 0.001$) as well as prediction model 25 and 100 ($p < 0.001$), but not between prediction model 50 and 100. We did not observe an increasing deviation between ADR and ADR_est over the study period.
**Conclusion:** ADR for subsequent colonoscopies of an individual endoscopist can be reliably predicted by using an individually calculated APDRR. It remains open to discussion at which time interval the individual APDRR should be calculated again. Although the mean RSME was low with the use of the averaged group APDRR, no significant correlation was found between ADR and estimated ADR for this model. Prospective studies would be valuable to verify this promising approach.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0729 REAL-LIFE MANAGEMENT OF ANTIPLATELET THERAPY (APT) PRIOR TO ENDOSCOPIC PROCEDURES: DOES DAILY PRACTICE FIT IN WITH GUIDELINES?

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**Introduction:** Despite the existence of several practice guidelines, there is a great amount of uncertainty regarding the periprocedural management of APT when a gastrointestinal endoscopy is scheduled.
**Aims & Methods:** Our objective was to describe the real periprocedural management of APT in outpatients undergoing upper and lower gastrointestinal endoscopies in our hospital, a tertiary referral center for the Valencian Region in Spain. To that purpose, consecutive outpatients scheduled for gastroscopy or colonoscopy in our Unit between January and June 2015 were surveyed. The referral note of each patient (which has a check box asking specifically for APT) was also reviewed. The collected variables were: age, gender, procedure, indication, referral doctoŕs specialty, APT status according to the information provided by the patient and by the referral note, APT indication, modification of APT prior to the procedure (stop/change), person responsible for this change and days of withdrawal if applicable.
**Results:** 668 patients were included [age (median, range) = 62 (19–99)] and 337 (50.5%) were male. A total of 685 procedures were performed (282 gastroscopies and 403 colonoscopies). Six patients underwent gastroscopy and colonoscopy in the same session; therefore 679 questionnaires were finally collected. According to the information provided by the patient, 102 patients (15%) were on APT; but according to the referral note, there were only 95 (14%). The information provided by the patient did not match that stated in the referral note in 37 cases (5.5%). Regarding the type of APT, there was a disagreement in 3 of the 81 patients (3.7%) who had information from both sources. Despite the specific check box, information about APT was lacking in 21 (3.1%) referral notes. Considering only the 95 patients whose referral note stated that they were taking APT, this therapy was modified before the procedure in 37 (39.1%). Specifically, acetylsalicylic acid (ASA) therapy was modified in 26 of 81 patients (32.1%), clopidogrel in 5 of 8 patients (62%), and DAPT in 6 of 6 patients (100%). In 11 of the 26 patients taking ASA (42.3%) the patient self-interrupted therapy, and in 15 (57.7%) a physician ordered the modification. On the other hand, a physician always ordered the modification of clopidogrel and DAPT. No relationship was shown between APT modification and neither the indication of APT (primary/secondary prophylaxis) nor the bleeding risk of the procedure. When a physician modified APT, ASA and clopidogrel were retired more than 5 days before the procedure in 12 (80%) and 4 cases (80%) respectively.
**Conclusion:** 1) The information about APT provided by the patient and the referral note does not match accurately; 2) ASA is interrupted in a significant proportion of cases, against guidelinés recommendations; 3) Physicians modify APT regardless of its indication and without considering the characteristics of the procedure; 4) APT is interrupted sooner than recommended by guidelines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0730 PREDICT, RESECT AND DISCARD – A QUANTITATIVE ASSESSMENT OF THE RISKS AND COST SAVINGS IN COLORECTAL CANCER SCREENING COMPARING TWO STRATEGIES FROM THE PORTUGUESE HEALTH SYSTEM

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**Introduction:** The "predict, resect and discard" (PRD) strategy, supported by the high diagnostic accuracy of the electronic chromoendoscopy technologies, has established new paradigms for diminutive colonic polyps management: polyps $\leq$5 mm can be resected and discarded without pathologic assessment and rectosigmoid hyperplastic polyps $\leq$5 mm can be left in place.
**Aims & Methods:** Cross-sectional analysis of a colorectal cancer (CRC) screening colonoscopy database (patients $\geq$50 years at average risk for CRC). Demographic and endoscopic data were collected. We intended to analyse up-front costs saving with the PRD strategy when applied to two different strategies of the Portuguese Health System (hospital cost – Governmental Order 234/2015 vs. community colonoscopy package – order of the Minister of Health of June 2015) and the impact in the surveillance intervals.
**Results:** A total of 284 colonoscopies (male-101) were performed in patients with a mean age of 61 years (50–75). Cecal intubation and adenoma detection rate was 97.2% and 27.5% (male: 39.6%; female: 20.8%), respectively. A total of 231 polyps (1–5) were documented in 132 patients: $\leq$5 mm n = 185, 5–9 mm n = 36, $\geq$10 mm n = 10; adenomas n = 120, HP n = 76, SSA n = 9, others n = 26. There were no CRC but 14 patients had high risk adenomas. Hospital cost: 64013.4€ (endoscopic procedure: 29642.5€ (46%), histological examination: 19847.3€ (31%)). Community cost: 47710.54€ (endoscopic procedure: 17341.04€ (36%), histological examination: 19847.3€ (42%)). By direct comparison, CRC screening in the community is 25% less expensive, mainly by reducing 42% the costs of the endoscopic procedure. The adoption of a PRD strategy would result in savings of 24% (15352€: polypectomies-2677€, histological evaluation-12675€) in the hospital regimen and 27% (12675.52€-histological evaluation) in the community package, without negative impact in the surveillance intervals (no villous elements or high-grade dysplasia in polyps $\leq$5 mm). By association the PRD strategy to the community package, total

CRC screening cost in this population would result in a savings of 35935.02€, meaning an overall saving of 45% in relation to the real cost.
**Conclusion:** PRD strategy is a promising approach to reduce costs in the CRC screening. Thus, it should be gathered efforts to the implementation and dissemination of the electronic chromoendoscopy technologies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0731 DIRECT PERORAL CHOLANGIOSCOPY BY USING A NEWLY DEVELOPED MULTIBENDING ULTRASLIM ENDOSCOPE FOR THE TREATMENT OF DIFFICULT BILE DUCT STONES

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**Introduction:** As direct peroral cholangioscopy (POC) by using an ultraslim endoscope provides direct visualization of the bile duct and allows performing of various therapeutic interventions more safely, several accessories have been developed to overcome low success rate of direct POC. In a recent, a multibending ultraslim endoscope was developed as a dedicated cholangioscope for direct POC.
**Aims & Methods:** The aim of this study was to evaluate the usefulness of direct POC by using a newly developed multibending ultraslim endoscope for lithotripsy in patients with difficult bile duct stone. A total of 20 patients, who were unsuccessfully treated for bile duct stones using conventional endoscopy, including mechanical lithotripsy (ML), underwent electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) under direct POC using a multibending ultraslim endoscope (Olympus Co., Tokyo, Japan). If a direct POC without accessory failed, an intraductal balloon (MTW Endoskopie, Wesel, Germany)-guided direct POC was performed. The success rate of complete stone removal and procedure-related adverse events were evaluated.
**Results:** A successful direct POC using a multibending ultraslim endoscope was achieved in all patients. The fragmentation of stone using 9 EHL or 11 LL was successful in 19 of 20 patients (95.0%). The complete stone removal was achieved in all patients (19/19). There were no procedure-related adverse events except one case of mild bleeding.
**Conclusion:** The direct POC by using a multibending ultraslim endoscope may be effective for the lithotripsy in patients with difficult bile duct stones.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0732 RAPID CARBAPENEMASE RESISTANT ENTEROBACTERIACEAE (CRE) PCR TESTING OF DUODENOSCOPES: FEASIBILITY AND ACCURACY

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**Introduction:** Duodenoscope-associated nosocomial transmission of CRE despite high-level disinfection (HLD) is an important health concern. Duodenoscope screening and surveillance by culture may reduce risk of patient exposure but culture is challenging to perform and may require 48–72 hours for results We evaluated the feasibility of testing a duodenoscope before and after manufacturer-recommended manual washing with a rapid PCR test for five genotypic markers of carbapenem resistance (CARBA-R, Cepheid, Sunnyvale, CA) after intentional exposure to three carbapenemase producing bacteria and compared results to culture.
**Aims & Methods:** The distal end of a research use TJF-Q180V duodenoscope (Olympus USA, Center Valley, PA) was immersed for 60 seconds in saline containing about 10e6 CFU per mL bacteria. The organisms (resistance gene) included *E. coli* (NDM), *K. pneumonia* (IMP), *P. aeruginosa* (VIM). During the exposure, the elevator was raised and lowered 10 times. The instrument was then air-dried for 24–48 hrs to mimic persistent contamination or incomplete washing and then a manufacturer-recommended manual washing including scrubbing the endoscope with a sponge in a cleaning agent (Metrizyme, Metrex, Orange, CA) and brushing the elevator and sampling ports, and flushing three times (>10 mL) with the cleaner was performed. The instrument was then rinsed briefly in water and soaked 10 seconds in ethanol (70%). The endoscope was then dried at least 60 minutes but up to 48 hours and sampled. Samples were collected by using a flocked swab (Copan, Murrieta, CA) dampened by saline, gently contacting a broad area around the terminus of the scope, including around the elevator shaft and sample port. The specimen swab was broken off into 10 mL saline and mixed by vortex for 10 seconds. The saline was then sampled with a second flocked swab which was dipped into the saline for 10 seconds and placed into the Cepheid CARBA-R processing buffer. The CARBA-R test was run according to manufacturer insert. A portion of the saline (0.05 mL) was plated to blood agar media and the remaining saline was placed into a blood culture bottle BACTEC/FX, BD, Sparks, MD). Three cycles of the above process were performed.
**Results:** Experiment 1: *E. coli* was used to contaminate the scope. At 24 hours a sample of the scope was culture negative and PCR positive. A manual cleaning was done and PCR and culture were both negative. Experiment 2: *Klebsiella pneumoniae* was used to contaminate the scope. At 48 hours a sample of the scope was culture and PCR positive. A manual cleaning was done and PCR and culture were both negative. Experiment 3: *Pseudomonas* was used to contaminate the scope. At 48 hours a sample of the scope was culture negative and PCR positive. A manual cleaning was done and PCR remained positive while culture was negative. After an additional 24 hours, another manual cleaning was done and PCR and culture were both negative.
**Conclusion:** CARBA-R PCR test is a potential method for rapid surveillance of carbapenemase producing organisms on endoscopes. PCR and culture were negative in all instances after manual cleaning and prior to HLD. Further study is required in the clinical setting to identify predictors of persistent contamination and to identify optimal sampling technique for endoscope surveillance.
**Disclosure of Interest:** F. Tenover: Dr. Tenover is an employee of Cepheid. Cepheid supplied the assay utilized in the study.
D. Persing: Dr. Persing is an employee of Cepheid. Cepheid supplied the assay utilized in the study.
All other authors have declared no conflicts of interest.

### P0733 SPYGLASS DIRECT VISUALIZATION SYSTEM VERSUS DIRECT PERORAL CHOLANGIOSCOPY USING BY A MULIBENDING ULTRASLIM ENDOSCOPE AS A SINGLE-OPERATOR PERORAL CHOLANGIOSCOPY FOR THE MANAGING BILIARY LESIONS: A PROSPECTIVE COMPARATIVE STUDY

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**Introduction:** Single-operator peroral cholangioscopy (POC) has been a new modality for diagnosis and treatment for various bile duct (BD) diseases. Up to date, SpyGlass direct visualization system (SpyGlass) and direct POC (DPOC) using ultra-slim endoscope have been used as a single operator POCs. However, there is no study to comparing two systems.
**Aims & Methods:** In this study, we prospectively compared the procedure success rate of POC using SpyGlass and DPOC for diagnosis and treatment of BD lesions. A total of 21 patients with BD lesions (diameter of CBD≥8 mm) requiring evaluation or treatment using POC were enrolled prospectively. All patients received POC using SpyGlass and mulibending ultraslim endoscope for DPOC. According to the presence of obstructive lesion, all patients were classified as obstructive type (8 patients) or non-obstructive type (13 patients), respectively. Technical and procedural success defined as abilities to visualize bifurcation / obstructive lesions and visualize target lesions / stone fragmentation, respectively.
**Results:** There was no significant differences between the SpyGlass and DPOC in technical success rates (100% vs. 95.2%, P = 0.485) and overall procedural success rate (71.4% vs.90.5%, P = 0.119).The procedural success rates of SpyGlass and DPOC were not different in 8 obstructive type (100%vs. 87.5%, P = 0.5). In 13 non-obstructive type, DPOC showed significantly higher procedural success rate (53.8% vs. 92.3%, P = 0.037). There was no significant difference between SpyGlass and DPOC groups in the success rates of targeted biopsy (80% vs. 100%, P = 0.385) and stone lithotripsy (100% vs. 75%, P = 0.5), respectively.
**Conclusion:** Both SpyGlass and DPOC demonstrated high technical success rates in patients with biliary lesions having dilated BD, but DPOC showed a higher procedural success for non-obstructive BD lesion. The POC using SpyGlass or DPOC according to the characteristics of BD lesion can be considered to improve the success rate of managing biliary lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0734 A COMPARATIVE STUDY OF STRATEGIES FOR PREVENTION OF POST-ERCP PANCREATITIS AFTER EARLY PRE-CUT SPHINCTEROTOMY FOR BILIARY ACCESS

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**Introduction:** Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is the most common serious ERCP complication. Needle knife precut sphincterotomy (PS) is used to achieve selective cannulation when standard techniques fail. It is associated with a higher risk of complications such as PEP, bleeding and perforation. It is frequently performed after a prolonged attempt at cannulation. If PS is performed early, a skillful endoscopist can avoid

papilla trauma from prolonged cannulation, and the risk of PEP may not be increased. Intravenous somatostatin infusion, rectal diclofenac and pancreatic duct (PD) stenting have been used to reduce the rate of PEP.
**Aims & Methods:** Aim: This study examined the effect of somatostatin, rectal diclofenac and PD stenting in reducing PEP in patients who underwent early PS to achieve selective common bile duct (CBD) cannulation. Methods: The data of patients in a prospective ERCP registry were reviewed. The study period was January 2006 to December 2015. A standardized approach to early PS had been implemented: 1) inadvertent guidewire cannulation of PD > 3 times; 2) presence of impacted CBD stone; 3) inability to achieve deep cannulation within 10 minutes. Patients with PS were enrolled. Exclusion criteria were patients who did not undergo PS and pancreatic ERCP. Measures used for PEP prophylaxis included: 1) none when there was minimal papilla trauma; 2) somatostatin infusion; 3) rectal diclofenac; 4) PD stent. The difference in rates of PEP between the different prophylactic strategies was analysed.
**Results:** During the study period, 2879 ERCP were performed, of which 191 had PS (mean age 66 years [range: 25–97]; 56.5% males). The most common diagnoses were CBD stones (138/191; 72.3%) and pancreatic adenocarcinoma (29/191; 15.2%). ERCP success rate after PS was 178/191 (93.2%). Post PS patients were divided into 4 groups: control with no intervention (57), somatostatin infusion (55), rectal diclofenac (55) and PD stent (24). The decision for not utilizing PEP measures in the first group was due to the endoscopist's assessment of minimal trauma to the papilla. PD cannulation occurred in 99/191 (51.8%). Overall the PEP rate was 6/191 (3.1%) and the severity was mild in all cases. PEP occurred in 6.1% of patients with PD cannulation but not in those without ($p = 0.016$). There was no statistically significant difference in PEP rates in the 4 groups. A trend towards lower rates was noted for the diclofenac and PD stent groups. The PEP rates were 1/57 (1.8%) in control, 4/55 (7.3%) with somatostatin, 1/55 (1.8%) with diclofenac and 0 with PD stent ($p = 0.209$). Post ERCP bleeding occurred in 3/191 (1.6%). There were no ERCP related perforation or mortality. The somatostatin group had significantly higher proportion of patients with guidewire cannulation of PD, compared to the control and diclofenac groups (65.5% vs. 35.1% vs. 34.5%, $p = 0.001$).
**Conclusion:** A strategy of early PS for biliary access was safe and effective. There was no significant difference in PEP rates whether or not prophylactic measures were adopted if there is minimal papilla trauma. A trend towards lower PEP rates was observed in patients who had either rectal diclofenac or PD stenting. These measures may be warranted in the presence of additional risk factors for PEP such as PD cannulation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0735 ENDOSCOPIC MINOR PAPILLA SPHYNCTEROTOMY IS EFFECTIVE FOR THE TREATMENT OF SYMPTOMATIC SANTORINICELE: LONG-TERM RESULTS IN A LARGE SERIES

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**Introduction:** Santorinicele (SC), a cystic dilatation of the intramural portion of the dorsal pancreatic duct, is a rare morphological alteration generally associated with pancreas divisum and acute recurrent pancreatitis. Endoscopic minor papilla sphyncterotomy (EPSm) has been proposed as treatment in few isolated cases or small series with encouraging results but never sistematically investigated.
**Aims & Methods:** The aim of this study is to assess the outcome of endoscopic treatment in a large series with long follow-up. From 2009 to 2015, at the tertiary care center of pancreatic disorders of Verona, 33 patients with SC and acute recurrent pancreatitis (APR) were enrolled for EPSm. The average number of pancreatitis before and after treatment was evaluated. Clinical outcome was analyzed and related with the secretin-enhanced magnetic resonance cholangiopancreatography (s-MRCP) findings performed before the endoscopic procedure. Mean follow-up after sphincterotomy was 41.4 months (range 12–80).
**Results:** The mean number of pancreatitis per year before and after endoscopic treatment was respectively 1.586 (95% CI 1.0548 – 2.1186) and 0.18 (95% CI 0.0029 – 0.3629). EPSm, performed in 30 patients, resulted effective in reducing the average number of pancreatitis ($p < 0.0001$). Only 1 (3.2%) severe EPSm related adverse event was observed (retroperitoneal perforation). Complete response was obtained in 86.6% of patients. Four patients relapsed after a mean time of 13 months from the sphincterotomy. In 3 of them we found another potentially cause of APR. No relation between clinical response and s-MRCP findings was observed.
**Conclusion:** SC, when associated with APR, represents an indication for endoscopic minor papilla sphincterotomy. This procedure is efficacy in reducing the recurrence of pancreatitis in 86% of cases. In non-responder patients, SC may represent a morphological finding not related with APR and another etiology must be searched.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0736 SPHINCTER OF ODDI DYSFUNCTION AFTER LIVER TRANSPLANTATION: EXPERIENCE IN A HIGH-VOLUME TRANSPLANT CENTER

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**Introduction:** Sphincter of Oddi dysfunction (SOD) in liver transplant (LT) recipients can occur 3–16% of patients, however there is scarce data regarding the specific characteristics, incidence, and long-term outcome of this condition. The aim of this analysis was to estimate the incidence and outcome of SOD in a cohort of LT recipients.
**Aims & Methods:** We reviewed 561 ERCP's performed in LT-patients with duct-to-duct biliary anastomosis at Hospital Clinic, Barcelona from 01/2003 to 01/2015. Information was obtained from electronic health records and a prospectively collected database. SOD in LT recipients was defined as the presence of cholestasis, elevated liver enzymes, dilated bile duct and absence of alternative diagnosis at ERCP. Patients with SOD underwent a biliary sphincterotomy with adequate drainage of contrast and bile. Definite SOD was defined as absence of alternative diagnosis in the following 12 months. Laboratory and clinical findings were obtained immediately before ERCP and 3 months post-ERCP to evaluate the effect of sphincterotomy.
**Results:** 1036 patients underwent LT from 2003 to 2015. 225 LT recipients underwent 561 ERCP's during the study period. Twenty-three patients met the initial criteria of SOD (10.2%). However, during the 12-month follow-up, 10 patients (43%) developed other conditions [biliary anastomotic stricture ($n = 1$), biliary sludge or stones ($n = 3$), chronic graft rejection ($n = 4$), HCV recurrence ($n = 1$) and chronic pancreatitis ($n = 1$)]. Therefore 13 of the 225 patients (5.8%) were diagnosed with definite SOD. Overall incidence was 1.2% among LT recipients. Patients with definite SOD had a significant decrease in bilirubin and alkaline phosphatase after sphincterotomy compared to those without SOD (Table). There were no complications after ERCP.

| | n | Lab enzymes | Pre-sphx | | Post-sphx | | p value |
|---|---|---|---|---|---|---|---|
| | | | Mean | SD | Mean | SD | |
| Definite SOD | 13 | Bilirrubin | 2.0 | 1.0 | 1.3 | 0.9 | .019 |
| | 13 | AP | 623.6 | 374.0 | 344.3 | 241.7 | .003 |
| | 13 | GGT | 378.0 | 240.4 | 245.0 | 266.8 | .087 |
| | 13 | AST | 58.9 | 28.2 | 65.8 | 40.4 | .701 |
| | 13 | ALT | 96.5 | 63.2 | 73.1 | 47.4 | .463 |
| Alternative diagnosis | 10 | Bilirrubin | 7.1 | 6.8 | 5.9 | 7.2 | .386 |
| | 10 | AP | 1357.1 | 995.0 | 1308.4 | 1115.7 | .878 |
| | 10 | GGT | 957.8 | 934.0 | 994.7 | 916.9 | .445 |
| | 10 | AST | 221.8 | 207.5 | 127.8 | 110.3 | .333 |
| | 10 | ALT | 221.2 | 178.7 | 93.3 | 48.3 | .074 |

Pre-Sphx, pre-sphincterotomy; Post-Sphx, post-sphincterotomy; SOD, sphincter of Oddi dysfunction; AP, alkaline phosphatase; GGT, gamma-glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine transaminase.

**Conclusion:** The estimated incidence of definite SOD in LT recipients was 1.2%. More than 40% of the patients with a suspected diagnosis of SOD at ERCP developed other conditions that accounted for cholestasis and abnormal liver enzymes. Biliary sphincterotomy is a safe and effective procedure in these cases as those with definite SOD had a resolution of cholestasis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0737 A PROSPECTIVE COMPARISON OF DIRECT DIGITAL AND BALLOON-ASSISTED CHOLANGIOSCOPY IN COMPLEX BILIARY DISEASE

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**Introduction:** Direct digital cholangioscopy (DDC) and balloon-assisted cholangioscopy (BAC) are important tools in the evaluation and management of complex biliary disease that have not been sufficiently compared.
**Aims & Methods:** OBJECTIVE: To assess the utility, indications, advantages and disadvantages of DDC compared with BAC in patients with complex biliary disease. METHODS: Prospective single centre observational study of all cholangioscopy procedures performed during a 10 month period (June 2015–April 2016) using either DDC (Spyglass® digital) or BAC (Olympus N180 gastroscope with 5FG MTW balloon). Strictures were dilated if required prior to cholangioscopy. Strictures were considered indeterminate if preceding cross-sectional imaging, and ERCP and/or EUS-acquired cytology or biopsies were negative for malignancy.
**Results:** 25 patients (28 procedures) had DDC and 17 patients (18 procedures) BAC. Median distal CBD diameters were similar, 6 mm in DDC group and 5 mm in BAC group. Cholangioscopy indications are shown in the Table. In general, DDC was used to investigate indeterminate hilar or intrahepatic strictures, particularly primary sclerosing cholangitis (PSC). Moreover, DDC-directed Holmium laser lithotripsy successfully fragmented 7 biliary (4 extrahepatic and 3 intrahepatic) stones but was unsuccessful in 1 pancreatic stone case. In addition, DDC enabled guidewire placement into poorly accessible intrahepatic segments for subsequent directed therapy or biopsies. However, BAC was usually preferred in extrahepatic biliary strictures because of superior optics and lower cost. Technical success rates were high (DDC 96% and BAC 94%) in both groups while median procedural times and biopsy yields were similar (Table). Complications rates were similar, occurring in 3 of 28 (10.7%) DDC procedures (2 cholangitis, 1 pneumonia) and 2 of 18 (11%) BAC procedures (1 cholangitis, 1 localized wire perforation).

**Table:** Indications and Procedural Details

| Indications | DDC (25 patients) | BAC (17 patients) |
|---|---|---|
| Indeterminate strictures: | | |
| - Extrahepatic | 4 | 9 |
| - Hilar and Intrahepatic (PSC) | 12 (7) | 7 (2) |
| Ampullary adenoma intraductal extension | 1 | 1 |
| Holmium laser lithotripsy | 8* | 0 |
| **Procedural Details** | | |
| Technical success / Total Procedures | 27/28 | 17/18 |
| Median procedural time, minutes (range) | 32 (20–82) | 24 (19–43) |
| Adequate histological specimen | 13/14 | 16/18 |
| Benign histology | 12/13 | 15/16 |
| Cholangioscopy-directed guidewire access | 6 | 0 |

*7 biliary and 1 pancreatic duct stone

**Conclusion:** In the era of direct digital cholangioscopy and balloon-assisted cholangioscopy: 1) Both are similar in terms of technical success rates, procedural time, tissue acquisition and complication rates; 2) DDC is particularly useful to manage intrahepatic strictures and for lithotripsy of complex stone disease; 3) Extrahepatic biliary strictures are usually best evaluated by lower-cost BAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0738 ERCP IN INFANTS, CHILDREN AND ADOLESCENTS IS FEASIBLE AND SAFE – RESULTS FROM A TERTIARY CARE CENTER

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**Introduction:** Indications for ERCP in children differ from adults, and concerns about potential lower effectiveness and more side effects limit the use of ERCP even in high volume centers. We retrospectively analyzed indications, effectiveness, limitations, and side effects of ERCPs in children $<18$ years.
**Aims & Methods:** From Jan 2012 – Mar 2015, 54 ERCPs (median 1, range 1–7) were performed in 31 children (mean age $7.6 \pm 6.1$ yrs; median weight 22 kg, range 3.3–142.7). Indications were suspected choledocholithiasis ($n = 13$), postoperative complications (15), ductal anomalies (14), tumors (10), and PSC (2). High-end ultrasonography and/or cross-sectional imaging was available for all patients before ERCP. All patients were followed up for at least 3 d.
**Results:** Therapeutic ERCP was performed in 36 children, diagnostic in 18, by adult ERCP expert endoscopists. Endoscopic papillotomy was performed in 16/54 examinations. General anesthesia was preferred, only in 6/54 interventions (in 16 to 17-years old), conscious sedation was used. In two patients, retrograde access to the papilla was necessary (after Roux-en-Y, duodenostomy). Successful intervention (defined as accurate diagnosis and/or adequate therapy) was possible in 87.0% (47/54 ERCPs), and was more often achieved in older children (mean age 10.9 vs. 4.2 years, median weight 34.0 vs. 8.3 kg). Standard duodenscopes were used in children $>20$ kg BW, smaller diameter duodenoscopes (min. diameter 7.5 mm, working channel 2 mm) in smaller children. Similarly, we used .018'', .025'', and .035'' wires. 5 complications were recorded (5/54, 9.3%), and included 4 cases of mild pancreatitis (7.4% PEP rate; incl. 2 pts. with aggravation of preexisting pancreatitis) and 1 aggravation of cholangitis in PSC despite antimicrobial prophylaxis. PEP was noted in 0 of 6 children with protective pancreatic stents vs. 4/43 without pancreatic stents. All complications were managed conservatively. No complications were attributed to mechanical stress on the GI tract.
**Conclusion:** ERCP in children only accounted for 3.3% of our ERCP caseload. Endoscopists must be aware of differing spectrum of pediatric biliary and pancreatic diseases. We underline this point by including the endoscopist and the pediatrician in the ERCP room. Failed cannulation was associated with small dimensions of young children. Accessories for small caliber duodenoscopes are limited, as is navigation at the papilla in babies. Complications were similar to rates reported in adults. Rectal NSAIDs in children were not yet standard in our cohort, but may be considered. Protective pancreatic stents were helpful but necessitate a second endoscopy or plain abdominal radiograph for stent removal or proof of spontaneous passage. In summary, ERCP in children appears to be safe and effective in selected indications. Close collaboration between endoscopists and pediatricians is necessary.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0739 COMPARISON OF MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY AND ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY IN DISEASE SEVERITY ASSESSMENT OF PRIMARY SCLEROSING CHOLANGITIS: IMPACT ON PROGNOSIS

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**Introduction:** Endoscopic retrograde cholangiography (ERC) has been considered as the gold-standard for the diagnosis of primaring sclerosing cholangitis (PSC), but it might have severe complications (e.q. pancreatitis)[1]. Magnetic resonance cholangiopancreatography (MRCP) is an accurate, cost-effective and non-invasive procedure for the diagnosis of PSC[2]. However, in the majority of the studies on the agreement MRCP-ERC, disease severity as well as the impact on the patients' prognosis was not been evaluated in detail.
**Aims & Methods:** Aims of the study were to evaluate: 1) the agreement between MRCP and ERC in the assessment of PSC severity 2) the impact of the imaging modality on the prognosis. PSC diagnosis was based on patient's history, laboratory findings, histology, ERC, MRCP and clinical follow-up. All PSC patients who underwent MRCP and ERC within 3-month interval ($n = 50$) were collected from PSC register of our hospital ($n = 614$). MRCP was done using either 1.5 Tesla (in 49) or 3 Tesla (10); 3D reconstruction was available in 56. Two gastroenterologists and two radiologists reviewed all ERC and MRCP imaging studies, respectively, by using the modified Amsterdam PSC score; a mean score for intra-hepatic (IH) and extra-hepatic (EH) bile ducts was calculated. The Kendall's tau-b test was used to measure pairwise correlation among the methods; weighted k for inter-rate agreement and the McNemar-Bowker Test to find out differences in between the methods. The prognosis (liver transplantation and death) was evaluated by January 2016.
**Results:** Overall, 59 MRCP and ERC (14 for diagnosis and 45 for follow-up) were performed in 50 patients (male 38, median age at diagnosis 31 years; 6–75) and included in the analysis. The median modified Amsterdam PSC score in

MRCP images was 3 for IH and 2 for EH bile ducts, whereas in ERC images was 3 for IH and 1 for EH bile ducts. The overall diagnostic accuracy in detecting any changes of PSC in IH was 98% (95%CI 91–100%) and in EH 81% (95%CI 69–90%). The agreement in describing disease severity was only fair for IH bile ducts (weighted k 0.347; 95%CI 0.162–0.531), Kendall's tau-b 0.395; SE 0.121, McNemar-Bowker Test p 0.193), especially for early stages of the disease. The agreement for disease severity was also only fair for EH bile duct changes (weighted k 0.305; 95%CI 0.158–0.452; Kendall's tau-b 0.440; SE 0.091; McNemar-Bowker Test p 0.002), especially for severe disease. By the end of follow-up, 10 patients were transplanted (4 for suspicion of malignancy and 6 for end-stage liver disease) and one patient died (cholangiocarcinoma). In these patients the agreement for IH was 91%. The agreement for EH was 64%; 4 patients (MRCP score severe changing and ERC score mild changes) were transplanted for end-stage liver disease.

**Conclusion:** The agreement between MRCP and ERC in detection of any PSC changes was good, but it turned out to be poor when assessing disease severity of bile duct changes. The relatively poor agreement (especially for EH assessment) seems to have an impact on prognosis. MRCP identified better severe EH changes, which related with complications. Future prospective studies confirming this finding are warranted.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0740 ENDOSCOPIC BILIARY STENT INSERTION THROUGH DUODENAL STENT IN PATIENTS WITH COMBINED MALIGNANT BILIARY AND DUODENAL OBSTRUCTION UNDER STENT OR PTBD GUIDANCE


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**Introduction:** Endoscopic stenting for combined malignant biliary and duodenal obstruction is technically demanding, especially in those with native papilla. However, this procedure can be facilitated when there is guidance from previously inserted stent or percutaneous transhepatic biliary drainage (PTBD) tube.

**Aims & Methods:** This study aimed to evaluate the feasibility and clinical success rate of endoscopic placement of biliary self-expandable metal stent (SEMS) through duodenal SEMS in patients with combined biliary and duodenal obstruction due to inoperable or metastatic periampullary malignancy. A total of 6 patients (4 male and 2 female) with combined malignant biliary and duodenal stricture underwent insertion of biliary SEMS through the mesh of duodenal SEMS from July 2012 to December 2015 at Korea University Ansan Hospital. All patients either had previously inserted biliary SEMS, plastic stent or PTBD for guiding insertion of biliary SEMS. M-duodenal (Bonastent, Korea) SEMS, a specialized SEMS with expandable lattices in the mid portion, were used for duodenal SEMS. Technical and clinical success rate, adverse events, and survival after completion of SEMS insertion were evaluated.

**Results:** The mean age of the patients was 56.3 years (range: 38–82 years). Half (n = 3) of the patients were diagnosed with pancreatic cancer and the remaining 3 patients had either gallbladder cancer (n = 1), ampulla of Vater cancer (n = 1) or common bile duct cancer (n = 1). The duodenal strictures were located in the first portion of the duodenum in 1 patient (type I), in the second portion in 3 patients (type II), and in the third portion in 2 patients (type III). Technical success rate of combined metallic stenting was 100%. Insertion of biliary SEMS was guided by previously inserted biliary SEMS in 4 patients, plastic stent in 1 patient, and PTBD in 1 patient. Clinical success rate was 83.3% (5/6). There were no early adverse events after the procedure. Mean survival period after combined metallic stenting was 118.6 days (range: 56–245 days).

**Conclusion:** Endoscopic placement of biliary SEMS through duodenal SEMS is feasible with high success rates and relatively easy when there is guidance from previously inserted biliary SEMS, pancreatic stent or PTBD. This method can be a good alternative for palliation in patients with combined biliary and duodenal obstruction.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0741 TRANSPANCREATIC SEPTOTOMY – AN ALTERNATIVE TO PRECUT FOR DIFFICULT BILIARY ACCESS?


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**Introduction:** Selective cannulation of the common bile duct (CBD) is an essential step in ERCP. However, this may not be achieved in up to 15% of patients. Techniques like precut have adequate success rates, but show higher risk of complications. Transpancreatic septotomy is an alternative facing difficult biliary access.

**Aims & Methods:** Our objective was to evaluate the efficacy and safety of transpancreatic septotomy when compared with precut technique. Between January-2014 and February-2016, alternative techniques to CBD cannulation were used in 70 patients (Septotomy-35 patients, Precut-35; Female-57.1%; Average age-69.5 ± 15.2 years-old). Several variables that could have influenced the success or complication rate were analyzed.

**Results:** The main indication for the procedure was choledocolithiasis, with or without cholangitis (67.2%), followed by CBD strictures (malignant-21.4%; benign-11.4%). The cannulation rate was 83.8% with septotomy and 76.5% with precut (p = 0.47). Biliary stone removal and stent placement was achieved in a similar percentage in both groups (p = 0.49 e 0.51, respectively), while the need to repeat ERCP in the next four months was higher with precut (p = 0.03). The complication rate was not different between the two techniques (17.1% vs. 23.5%; p = 0.51). However, they were more severe with precut, as two patients died following the procedure.

**Conclusion:** These techniques are useful when there is difficult billiary access and obtained a similar success rate. However, there was a lower need to repeat the procedure after performing septotomy. Complication rate was also similar, but more severe outcomes occurred with precut.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0742 INTERNATIONAL MULTICENTER COMPARATIVE TRIAL OF ENDOSCOPIC ULTRASONOGRAPHY GUIDED GASTROENTEROSTOMY VERSUS SURGICAL GASTROJEJUNOSTOMY FOR THE TREATMENT OF MALIGNANT GASTRIC OUTLET OBSTRUCTION


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**Introduction:** There are limitations to enteral self-expandable metallic stents (SEMS) and surgical gastrojejunostomy (SGJ) in the treatment of patients with malignant gastric outlet obstruction (GOO). EUS-guided gastroenterostomy (EUS-GE) is a novel procedure that potentially offers long-lasting luminal patency without the risk of tumor ingrowth/overgrowth, while avoiding the morbidity of a surgical procedure. Currently there are no studies comparing EUS-GE to SGJ.

**Aims:** To compare the clinical success, technical success, adverse events (AEs), length of hospital stay (LOHS) and reintervention rates in EUS-GE versus SGJ.

**Methods:** This was a multicenter international retrospective comparative study of EUS-GE and SGJ in patients with malignant GOO who underwent either EUS-GE at 6 centres (3 US, 2 Europe, and 1 Asia) between 2013 and 2015 or SGJ at 1 US centre between 2008 and 2010 for the management of GOO. EUS-GE was performed using lumen apposing stents.

Technical success was defined as adequate positioning and deployment of the stent as determined by the endoscopist and confirmed radiographically. Technical success of SGJ was defined as technical feasibility to perform a gastrojejunostomy, clinical success as the ability to tolerate oral intake without vomiting. The need for reintervention (repeat endoscopic or surgical procedures due to recurrent GOO symptoms) was considered a surrogate for recurrent GOO.

**Results:** A total of 93 patients with malignant GOO treated with either EUS-GE (n = 30, 57% men, mean age 70 ± 13.3 year) or SGJ (n = 63, 52% men, mean age 68 ± 9.6 year) were identified: Etiology of GOO was most commonly due to pancreatic cancer (n = 70), followed by ampullary cancer (n = 11), gastric cancer (n = 5), duodenal cancer (n = 1), metastatic cancer (n = 4) and gallbladder cancer (n = 2)). Most patients presented with weight loss (n = 90, 97%) with an average of 6.8 kg (range 2–20.4) loss per patient. The most common location of GOO was at second part of the duodenum (n = 72, 77%). Peritoneal carcinomatosis was present in 13 (43%) patients in the EUS-GE group and 7 (11.12%) patients in the SGJ group (p = 0.001). Although technical success was significantly higher in the SGJ group as compared to the EUS-GJ group (100% vs. 87%, OR 3.4, p = 0.009), clinical success was similar between both groups (90% vs. 87%, OR 1.7, 95%CI (0.44–7.07), p = 0.18). Although rate of AEs was lower in the EUS-GE group, the difference was not statistically significant (16% vs 25%, p = 0.3). The mean LOHS was similar in the EUS-GE group compared to SGJ (11.6 days ± 6.6 vs. 12 days ± 8.2 days,

P = 0.35). The mean length of follow-up was similar in both groups (107.8 ± 70 days in EUS-GE vs. 73.7 ± 156 days in SGE, p = 0.79). Reintervention rate were also not different between the two groups (3% vs. 9%, p = 0.3). Similarly, the mean time to reintervention was similar (88 days vs. 179 days, p = 0.83).

| | EUS-GE (n = 30) | Surgical GJ (n = 63) | p value |
|---|---|---|---|
| Technical success, n (%) | 26 (87) | 63 (100) | 0.009 |
| Clinical success, n (%) | 26 (87) | 57 (90) | 0.18 |
| Re-intervention, n (%) | 1 (3) | 6 (9) | 0.9 |
| Adverse events, n (%) | 5 (16) | 16 (25) | 0.3 |
| Mean length of hospitalization (days), mean±SD | 11.6 ± 6.6 | 12 ± 8.2 | 0.35 |

**Conclusion:** EUS-GE is associated with equivalent efficacy and safety as compared to surgical GJ. This is the first comparative trial between both techniques suggests EUS-GE as a non-inferior but less invasive alter to surgery. Prospective comparative trial is needed to confirm these intriguing results.
**Disclosure of Interest:** M. Khashab: Dr. Khashab is a consultant for Boston Scientific. All other authors have no relevant disclosures.
All other authors have declared no conflicts of interest.

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### P0743 INTEROBSERVER AGREEMENT AMONGST EXPERT ACADEMIC AND NON-ACADEMIC PATHOLOGISTS FOR THE NEW 20 GAUGE PROCORE BIOPSY NEEDLE; A PROSPECTIVE MULTICENTER STUDY OF 74 CASES


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**Introduction:** The first report on the performance of a recently introduced flexible 20 gauge ProCore biopsy needle was promising, with a diagnostic yield of >85% (1). However, prior to implementation of this device, its reproducibility should be established, not only in the hands of academic experts, but also in non-academic practice.
**Aims & Methods:** To evaluate the interobserver agreement amongst expert and non-academic pathologists in grading the quality and diagnostic value of specimens obtained with the new flexible 20 G ProCore FNB needle (Cook Medical, Limerick, Ireland). Five international EUS-centers prospectively collected 74 samples (39 solid pancreatic masses and 35 lymph nodes) using the new needle. All samples were independently reviewed by five expert academic and five non-academic pathologists for sufficiency of tissue quality, percentage of target cells present, presence of tissue cores, suitability for additional analysis (i.e. immunohistochemistry), and diagnostic classification (non-diagnostic, benign, neoplastic, or malignant). Agreement was calculated using the Fleiss' kappa statistic and 95% confidence intervals (CIs).
**Results:** Overall, 91% of cases were considered to be of sufficient quality, with moderate agreement among the ten reviewing pathologists ($\kappa = 0.49$, table 1). Agreement was higher within the group of expert academic pathologists (p = 0.02). Interobserver agreement on the diagnostic classification was good amongst both academic ($\kappa = 0.62$; 95% CI 0.57–0.67) and non-academic pathologists ($\kappa = 0.59$; 95% CI 0.55–0.64). Regarding sample quantity, tissue cores were considered present in 70% of cases ($\kappa = 0.37$), with a higher level of agreement among expert pathologists ($p < 0.001$). As for cellularity of the sample, presence of ≥50% of target cells was reported in 78% of cases ($\kappa = 0.31$). In addition, suitability for additional analyses was rated as positive in the majority of samples (76%), with higher agreement among expert academic pathologists ($p < 0.001$). When comparing pancreatic to lymph node samples, agreement on the diagnostic classification was higher for lymph nodes ($\kappa = 0.64$; 95% CI 0.61–0.67) than for pancreatic masses ($\kappa = 0.54$; 95% CI 0.51–0.58, $p < 0.001$). In addition, lymph node specimens provided higher agreement with regard to possibility for additional analysis ($\kappa = 0.51$; 95% CI 0.46–0.56 versus $\kappa = 0.38$; 95% CI 0.33–0.43, $p < 0.001$). Agreement on specimen quality was higher for pancreatic samples ($\kappa = 0.62$; 95% CI 0.57–0.67 versus $\kappa = 0.43$; 95% CI 0.38–0.48, $p < 0.001$).
**Conclusion:** There was good interobserver agreement amongst both expert academic and non-academic pathologists in the assessment of the quality and diagnostic value of specimens obtained with the new 20 gauge ProCore biopsy needle. Follow-up data is required to confirm the diagnostic accuracy of this agreement.
**Disclosure of Interest:** M.J. Bruno: Lecturer and consultant for Cook Medical and Boston Scientific.
All other authors have declared no conflicts of interest.

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### P0744 EUS-GUIDED HEPATICO-GASTROSTOMY VS PERCUTANEOUS TRANSHEPATIC DRAINAGE FOR MALIGNANT BILIARY OBSTRUCTION AFTER FAILED ERCP


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**Introduction:** Percutaneous transhepatic biliary drainage (PTBD) is widely performed as a salvage procedure in patients with unresectable malignant

**Table 1. (P0743):** Rates for sample quality, percentage of target cells, presence of tissue cores, possibility to perform additional analysis, diagnostic classification, and $\kappa$-statistics for all ten pathologists and for academic versus non-academic pathologists.

| Scored variables | All pathologists (N = 10) | Academic (N = 5) | Non-academic (N = 5) |
|---|---|---|---|
| **Sufficient quality (%)** Agreement $\kappa$ (95% CI) | 91 0.49 (0.46–0.53)) | 90 0.51 (0.43–0.58) | 92 0.42 (0.35–0.49) |
| **Target cells ≥50% (%)** Agreement $\kappa$ (95% CI) | 68 0.31 (0.28–0.34) | 61 0.33 (0.26–0.40) | 74 0.27 (0.20–0.34) |
| **Tissue core present (%)** Agreement $\kappa$ (95% CI) | 70 0.37 (0.34–0.41) | 71 0.41 (0.34–0.48) | 68 0.26 (0.19–0.33) |
| **Additional analysis possible (%)** Agreement $\kappa$ (95% CI) | 76 0.47 (0.43–0.50) | 79 0.51 (0.44–0.58) | 73 0.38 (0.30–0.45) |
| **Diagnostic classification (%)** Non-diagnostic Benign Neoplastic Malignant Agreement $\kappa$ (95% CI) | 12 10 20 59 0.61 (0.60–0.64) | 12 10 21 57 0.62 (0.57–0.67) | 11 9 19 60 0.59 (0.55–0.64) |

CI: confidence interval.

obstruction of the common bile duct after failed endoscopic retrograde cholangiopancreatography (ERCP) or in case of surgically altered anatomy. Endoscopic ultrasound-guided Hepaticogastrostomy (EU-HGS) is a more recently introduced alternative to relieve malignant obstructive jaundice
**Aims & Methods:** The aim of this prospective observational study was to compare the outcome, efficacy and adverse events of EU-HGS and PTBD. From April 2012 to August 2015, consecutive patients with malignant bile duct obstruction who underwent EU-HGS or PTBD in two tertiary-care referral centers were included. The primary endpoint was the clinical success rate. Secondary endpoints were technical success, overall survival, procedure-related adverse events, incidence of adverse events, and reintervention rate.
**Results:** Fifty-one patients (EU-HGS n = 31, PTBD, n = 20) were included. Median survival was 71 days (range 25–75th percentile; 30–95) for the EU-HGS group and 78 days (range 25–75th percentile; 42–108) for PTBD group (p = 0.99). Technical success was achieved in all patients in both groups. Clinical success was achieved in 25 (86%) of 31 patients in the EUS-HPG group and in 15 (83%) of 20 patients in the PTBD group (p = 0.88). There was no difference of adverse events rates between 2 groups (EU-HGS: 16%; PTBD: 10%)(p = 0.69). Four deaths within one month (2 hemorragic and 2 septic) were considered procedure-related (2 in EU-HGS group and 2 in PTBD group). Overall reintervention rate was significantly lower after EU-HGS (n = 2) than after PTBD (n = 21) (p = 0.0001). Length of hospital stay was shorter after EU-HGS (15 days vs 22 days; p = 0.002).
**Conclusion:** EU-HGS can be an effective and safe mini invasive procedure alternative to PTBD with similar success and adverse events rate but a lower number of reintervention and length of hospitalization.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0745 ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE FOR MALIGNANT BILIARY OBSTRUCTION AFTER FAILED ERCP: A SINGLE ITALIAN CENTER EXPERIENCE

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**Introduction:** Endoscopic ultrasonography-guided biliary drainage (EGBD) has been proposed as an alternative drainage technique for percutaneous transhepatic biliary drainage (PTBD) in patients with obstructive jaundice where endoscopic retrograde cholangiopancreatography (ERCP) has failed.
**Aims & Methods:** All patients afferent to Santa Maria Nuova Hospital in Reggio Emilia, between January 2011 and March 2016, with malignant obstructive jaundice, in whom ERCP had failed, were enrolled. Inclusion criteria are: patients over 18 years old, malignant bile duct obstruction with unsuccessful ERCP drainage. Patients with benign stricture were excluded. The end points were to evaluate technical and clinical success rate, adverse events rate and follow-up of direct transluminal EGBD. Technical success was defined as success of stent placement in the desired location. Early clinical success was defined as a drop in the bilirubin level by 50% at 2 weeks and late clinical success as a drop to below 3 (level that allows patients to undergo chemotherapy) at 4 weeks.
**Results:** In this study we enrolled 29 patients (11 men; median age 72; interquartile range, 61 to 90) underwent EGBD: 21 by intrahepatic approach (IA), 8 extraepatic approach (EA) The reason for EGBD was obscured ampulla by invasive cancer in 37.9% (11/29), postsurgical anatomy in 31.0% (9/29), failed deep biliary cannulation in 24.1% (7/29), hepaticojejunostomy stricture in 3.4% (1/29) and gastric outlet obstruction in 3.4% (1/29). EUS-guided cholangiography was successful and confirmed a distal common bile duct stricture in 26 patients (90%). Technical success in EGBD was achieved in 82.7% (24/29) of patient with a successful cholangiography: 90.5% in IA and 62.5% in EA. Early clinical success was reached in 62.1% (66.7% IA, 50% EA) and late clinical success in 39.9% (38.1% IA, 37.5% EA). Median bilirubin value decrese from 16.5 to 5.1 mg/dl after the procedure. Stent dysfunction occurred in 6 cases (20.6%) while procedure-related severe adverse event occurred in 3 patients (10.3%) with several comorbidities that developped severe cholangitis and died after 3–16 days after the procedure from multiorgan failure
**Conclusion:** EGBD is a safe and effective procedure to provide biliary access and drainage after failed ERCP. EGBD provides a viable alternative to PTBD, and limited available data suggest equivalent efficacy and safety.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0746 ACCURACY OF QUALITATIVE ENDOSCOPIC ULTRASOUND-GUIDED ELASTOGRAPHY FOR THE DIAGNOSIS OF MALIGNANCY OF LEFT ADRENAL GLAND MASSES

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**Introduction:** Endoscopic ultrasound (EUS) is a useful tool for the evaluation of the left adrenal gland, mainly in the context of the staging of lung cancer. Endoscopic ultrasound (EUS)-guided elastography evaluates the stiffness of different tissues, which has been shown to be highly accurate for the diagnosis of malignancy of solid pancreatic lesions and lymph nodes.
**Aims & Methods:** Aim of our study was to evaluate the accuracy of EUS-guided elastography for the diagnosis of malignancy of left adrenal solid lesions.
**Methods:** 32 consecutive patients (mean age 66.1 years, range 46–80, 20 male), who underwent EUS-guided elastography for the evaluation of solid left adrenal lesions over the last 4 years were identified from a prospectively collected endoscopy database, and included in the study. EUS-guided elastography was performed using a convex array echoendoscope (Pentax EG-3870UTK and EG-3270UK), and the HITACHI-PREIRUS and ASCENDUS ultrasound equipment. The elastographic pattern was qualitatively evaluated based on color predominance (green or blue). Final diagnosis was based on surgical histopathology or, in non-operated cases, on EUS-guided fine needle biopsy, imaging assessment (CT scan and/or PET scan), with a minimum clinical follow-up of 6 months. Probability of malignancy according to the elastographic pattern is described.
**Results:** Mean size of left adrenal masses was 31.4 ± 16.8 mm. Malignancy was confirmed by reference methods in 20 cases, whereas the remaining 12 left adrenal masses were finally considered as benign. Three different elastographic patterns were identified: 1) heterogeneous blue-predominant pattern (n = 21), 2) heterogeneous green-predominant pattern (n = 10), and 3) heterogeneous mixed green-blue pattern with geographical appearance and no color predominance (n = 1). Nineteen out of the 20 malignant lesions (95%) showed a blue-predominant pattern; the remaining malignant lesion showed a green-predominant pattern. Nine out of the 12 benign lesions (75%) showed a green-predominant pattern, two showed a blue-predominant pattern, and one had a mixed green-blue pattern. The probability of malignancy of a left adrenal mass showing a blue-predominant pattern is of 91.3%, whereas is as low as 10% in the presence of a green-predominant pattern.
**Conclusion:** EUS-guided elastography is a useful tool for the differential diagnosis of left adrenal masses. It provides specific colour patterns supporting the malignant or benign nature of the lesions.
**Disclosure of Interest:** J.E. Domínguez-Muñoz: International advisor Pentax
All other authors have declared no conflicts of interest.

## P0747 COMPARISON OF SPECIMEN ADEQUACY AND DIAGNOSTIC PERFORMANCES ACCORDING TO EUS-FNA TECHNIQUES IN PANCREATIC LESIONS: NO SUCTION, SUCTION AND CAPILLARY SUCTION

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**Introduction:** Different types of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) techniques are used in clinical practice. However, controversy still remains as to which EUS-FNA techniques would result in better adequate specimen and diagnostic accuracy. The aim of our study was to compare specimen adequacy and diagnostic performances according to EUS-FNA techniques (no suction vs. suction vs. capillary suction) in a same patient with pancreatic lesions.
**Aims & Methods:** Patients who referred to EUS-FNA for pancreatic mass lesion were enrolled. Basically, we performed EUS-FNA with three needle passes and applied each pass of different FNA techniques (suction, no suction or capillary suction) which were randomly allocated. Additional needle passes were allowed to obtain an adequate specimen after the initial three needle passes without adequate specimen. EUS-FNA specimens were evaluated by one experienced cytopathologist who was blinded to which EUS-FNA techniques were applied. The specimen adequacy and diagnostic performances for malignancy were compared among EUS-FNA techniques.
**Results:** From Jan. 2014 to Oct. 2015, 113 patients with pancreatic mass were enrolled and 4 patients were excluded due to loss of follow-up after EUS-FNA. Finally, 109 patients (65 males; median age, 67 years) with 327 needle passes were included without technical failure. The cumulative diagnostic accuracy for

**Table (P0748)**

| | | Standard classification 3–4 criteria | 3–4 criteria | >6 criteria |
|---|---|---|---|---|
| Rosemont classification | Indeterminate | 106 (100%) p = 1<br>Rho = 0.9229 | 0 (0%) p = 0.2623<br>Rho = 0.656 | 0 (0%) p = 0.000<br>Rho = 0.3422 |
| | Suggestive | 10 (7.69%) p = 0.3882<br>Rho = 0.599 | 115 (88.46%) p = 0.2207<br>Rho = 0.832 | 5 (3.83%) p = 0.000<br>Rho = 0.314 |
| | Consistent | 1 (1.85%) p = 0.000<br>Rho = 0.375 | 9 (16.67%) p = 0.000<br>Rho = 0.252 | 44 (81.48%) p = 0.1967<br>Rho = 0.8244 |

malignancy for overall needle passes was 61.5%, 84.4% and 91.7% at 1st, 2nd and 3rd pass, respectively. Although high rate of inadequate specimen in EUS-FNA with capillary suction was occurred, there was no significant differences among EUS-FAN techniques and number of needle pass. EUS-FNA with no suction at 2nd needle pass showed statistically high rate of diagnostic accuracy comparing to suction at 2nd pass and no suction at 1st and 3rd pass (P = 0.016, 0.051, 0.034).
**Conclusion:** EUS-FNA with no suction, suction and capillary suction showed similar rate of inadequate specimen. However, further prospective study including variable lesions is needed to validate for optimal application and sequences of EUS-FNA techniques.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0748 CONCORDANCE BETWEEN THE ROSEMONT AND THE STANDARD ENDOSCOPIC ULTRASOUND CLASSIFICATION OF CHRONIC PANCREATITIS

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**Introduction:** Endoscopic ultrasound (USE) is considered the most sensitive technique for the diagnosis of chronic pancreatitis (CP). However, EUS has less than optimal interobserver agreement for the diagnosis of CP. To minimize this inconvenience, two EUS-based classifications are used: the standard classification, which is based on the simple scoring of EUS criteria of the disease (4 parenchymal and 5 ductal), and the Rosemont classification, which includes weighted EUS criteria and stricter definitions for individual features to establish four groups of patients (normal, indeterminate, suggestive and consistent with CP). Aim of our study was to evaluate the concordance between the Rosemont and the standard EUS classifications for the diagnosis of different stages of CP.
**Aims & Methods:** Aim of our study was to evaluate the concordance between the Rosemont and the standard EUS classifications for the diagnosis of different stages of CP.
Methods: Retrospective analysis of a prospectively collected database. CP patients who underwent a EUS between October-2014 and November-2015 were included. EUS was performed by linear Pentax echoendoscopes (EG-3870UTK y EG-3270UK) and HITACHI-ASCENDUS ultrasound equipment. Standard EUS criteria and Rosemont classification of CP were recorded. Data were analyzed by McNemar-test and Spearman correlation-test.
**Results:** 290 patients (mean age 53 years, range 41–61, 222 male) met the inclusion criteria. Table shows patient distribution based on standard and Rosemont criteria, as well as the concordance and correlation between the two classifications. The majority of patients classified as indeterminate, suggestive and consistent with CP according to the Rosemont classification presented 3–4, 5–6 or >6 criteria, respectively. Concordance between the two classifications is lower at advanced stages of the disease due to the mischaracterization of standard parenchymal criteria in the presence of calcifications.
**Conclusion:** Standard and Rosemont EUS classifications of CP correlates significantly at early and moderate stages of the disease. The standard classification does not allow a proper scoring of EUS findings in patients with chronic calcifying pancreatitis.
**Disclosure of Interest:** J.E. Domínguez-Muñoz: International Advisor Pentax
All other authors have declared no conflicts of interest.

## P0749 IMPACT OF VISUAL ON-SITE EVALUATION DURING ENDOSCOPIC ULTRASOUND ON FINE NEEDLE ASPIRATION CYTOLOGY

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**Introduction:** Rapid on site evaluation (ROSE) has a deeper impact on Endoscopic Ultrasound (EUS)-guided fine needle aspiration (FNA) adequacy rate[1–2], but a cytopathologist on site is not available in all endoscopic centers. Macroscopic on-site evaluation (MOSE) was suitable to estimate the adequacy of the histologic core specimen obtained by EUS-FNA using a 19-G needle but often a thinner needle is preferred to perform EUS-FNA[3–4].
**Aims & Methods:** The aim of this study was to assess the efficacy of Visual On Site Evaluation (VOSE) in estimating the adequacy of FNA cytological specimens.
Thirty-three patients underwent EUS-FNA for pancreatic solid lesion or for enlarged lymph nodes with 22-or 25-Gauge (G) needle. VOSE was performed assessing each FNA pass in a fixative prepared fluid, evaluating: 1. blood (Ba, absent; B-, little; B+, a lot); 2. macroscopic visible core (MVC), single or multiple, long (>4 mm) or short (≤4 mm), red or white; 3. necrotic or fibrinoid material. When the macroscopic core was absent, the sample was considered inadequate.
**Results:** A total of 125 FNA needle passes was performed: 33 using 22-G and 92 passes using 25-G needle; 100 passes on pancreatic lesions, 25 on lymph nodes. Mean(SD) of needle passes was 3.47(0.81). VOSE results are summered in table 1. Correspondence between VOSE and cytological adequacy was of 91.2%. There was no concordance for 11 samples: 2 samples were adequate for VOSE but inadequate for the cytopathologist and 9 samples were inadequate for VOSE but adequate for the cytopathologist.

**Table 1.:** VOSE results

| | |
|---|---|
| **Presence of blood**, n (%), Ba/B-/B+ | **35**(28)/ **60**(48)/ **30**(24) |
| **Presence of MVC**, n (%) | **107**(85.6) |
| **Single/Multiple**, n (%) | **51**(48)/ **56**(52) |
| **Short/Long**, n (%) | **46**(43)/ **61**(57) |
| **Red/White**, n (%) | **60**(57)/ **47**(43) |
| **Presence of necrosis**, n (%) | **16**(12.8) |

**Conclusion:** VOSE can be an easy and feasible indicator of EUS-FNA adequacy when ROSE is not available
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0750 IN VIVO CHARACTERIZATION OF ABNORMALITIES IN SMALL BOWEL DISEASES USING PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY

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**Introduction:** Probe-based confocal laser endomicroscopy (pCLE) enables real-time optical biopsy.
**Aims & Methods:** Little is known about the pCLE imaging deep inside the small bowel, therefore we determined its usefulness. Between April 2014 and January 2016, we performed 38 pCLE examinations during double-balloon enteroscopy with intravenous fluorescein in 37 patients with: tumors (n = 10), vascular disorders (n = 6), inflammatory diseases and drug injuries (n = 13), other disorders (n = 4), and normal findings (n = 4). We measured the calibers of capillary and lymphatic vessels at 15 different sites each and compared calibers between pCLE images and histopathology. We also compared pCLE findings with pathologic diagnosis.
**Results:** The inner diameters of capillary vessels beneath the epithelium and in the middle of villi were $16.2 \pm 3.0$ mm and $14.5 \pm 3.1$ mm, respectively, in the pCLE images but were not consistent with formalin-fixed paraffin-embedded histology. In tumors, larger capillary vessels were observed in aggressive malignant lymphoma and metastasis, and a "soccer ball-like pattern" constituting homogenous dark cells packed by polygonal, narrower capillary vessels was characteristic in pCLE images of a malignant lymphoma follicle. Hereditary hemorrhagic telangiectasia and angiodysplasia contained anastomosis of capillary vessels of different calibers. In IgA vasculitis, segmental capillary strictures were observed. Intestinal lymphangiectasia with protein-losing enteropathy contained a reticular network of lymphatic vessels and dilated lymphatic ducts accompanied by numerous cell gaps. pCLE findings corresponded to pathologic diagnosis in 32 examinations (94%).
**Conclusion:** pCLE was useful for in vivo detection of abnormalities of the capillary and lymphatic vessels and epithelium and the diagnosis in various small bowel diseases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0751 DOUBLE-BALLOON COLONOSCOPY: A 7-YEAR EXPERIENCE FROM EDINBURGH

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**Introduction:** In experienced hands, conventional colonoscopy fails to achieve caecal intubation in around 5% of patients, mainly due to anatomical factors and/or patient tolerance [1–3]. Recently, it has been reported that double-balloon colonoscopy (DBC) is effective in completing colonic examination in such cases [1,4]. This retrospective study aims to present the utility of DBC from a tertiary care centre in South East Scotland.
**Aims & Methods:** Retrospective study; consecutive patients who underwent DBC without general anaesthesia from Dec 2008–Dec 2015, following incomplete colonoscopy, were included. Information extracted from case notes for initial colonoscopy: indication(s), patient clinical characteristics, procedure data, pathology found, therapeutic interventions and reason for failure to complete examination; and, for DBC: caecal intubation rate, pathology found, endoscopic interventions performed, sedation used and complications. Data are reported as mean (±SD) or median (range).
**Results:** Over the study period, DBC was performed in 57 patients (31 F/26 M; median age 62.9, range 20–89 years). Indications for colonoscopy were obscure GI bleeding in 14 (24.5%), prior abnormal cross-sectional imaging in 4 (7.0%), known or suspected polyps in 21 (36.8%), investigation or surveillance of inflammatory bowel disease in 12 (21.1%), and/or cancer screening in 4 (7.0%). 16/57 (28.1%) patients had previous abdominal or pelvic surgery. 19/57 (33.3%) patients had 2 or more previous failed colonoscopies. Reasons for failure of previous colonoscopies were: technical difficulties (excessive looping/tortuous colon, long colon) (n = 34), patient discomfort (n = 13), fixed angulated colon (n = 5) and/or severe diverticulosis (n = 3). With DBC, caecal intubation was achieved in 55/57 (96.5%) patients. In 29 (50.9%) patients, DBC revealed significant pathology; the majority of these findings 79.3%(23/29) were inaccessible by conventional colonoscopy. Therapeutic interventions (endoscopic mucosal resection, Argon Plasma Coagulation and/or polypectomy) were performed in 22/57 (38.6%) patients. For sedation, the midazolam dose was $2.94 \pm 1.6$ mg and that of Fentanyl $70 \pm 40\,\mu$g; comparable to previous data from our centre [5]. No complications occurred during DBC.
**Conclusion:** DBC is highly effective for completing colonic evaluation in patients with previous incomplete colonoscopy. DBC should be considered as the modality of choice in patients with incomplete colonoscopy in whom follow-up imaging suggests the presence of significant proximal colonic pathology, and as a useful option in any patient in whom standard colonoscopy has been incomplete [3].
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0752 EFFICACY AND SAFETY OF URGENT DOUBLE BALLOON ENTEROSCOPY-ASSISTED ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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**Introduction:** Endoscopic retrograde cholangiopancreatography (ERCP) in patients with altered gastrointestinal anatomy is challenging. The development of short double balloon enteroscopy (DBE) enabled deep access to the blind end of the intestine to perform ERCP. Although ERCP using DBE (DB-ERCP) is an established technique, there have been no reports on the efficacy and safety of DB-ERCP when acute biliary decompression is required.
**Aims & Methods:** The aim of this study was to evaluate this procedure in the urgent care setting. Between July 2007 and January 2016, we performed 144 DB-ERCP procedures in 79 patients with altered anatomy (77 procedures with Roux-en-Y gastric bypass (RYGB), 16 with Billroth II gastrectomy (B-II), 17 with pancreatoduoderectomy (PD), and 6 with pylorus preserving pancreaticoduodenectomy (PPPD), 9 with hepaticojejunostomy, 19 with other procedures). We defined urgent DB-ERCP as performance of the procedure within 24 hours of the diagnosis of pancreaticobiliary disease and nonurgent DB-ERCP as performance of the procedure 24 hours or more after the diagnosis. We retrospectively evaluated the success rate of reaching the blind end, the therapeutic success rate and the occurrence of complications in urgent and nonurgent DB-ERCP.
**Results:** We performed 30 urgent DB-ERCP procedures (28 patients) with altered anatomy (23 with RYGB, 3 with PD, 1 with hepaticojejunostomy, and 3 with other procedures) and 114 nonurgent DB-ERCP procedures (51 patients) with altered anatomy (54 with RYGB, 16 with B-II, 14 with PD, 6 with PPPD, 8 with hepaticojejunostomy, and 16 with other procedures). In urgent DB-ERCP, successful deep insertion of the endoscope to the blind end was accomplished in 27 of 30 procedures (90.0%). Deep biliary cannulation was successful in 21 of 27 procedures reaching the blind end (77.8%). Therapeutic intervention was achieved in all of 21 procedures in which deep biliary cannulation was successful (100%). The overall intention to treat therapeutic success rate was 70%. In nonurgent DB-ERCP, successful deep insertion of the endoscope to the blind end was accomplished in 102 of 114 procedures (89.5%). Deep biliary cannulation was successful in 91 of 102 procedures reaching the blind end (89.2%). Therapeutic intervention was achieved in 90 of 91 procedures in which deep biliary cannulation was successful (98.9%). The overall intention to treat therapeutic success rate was 78.9%. Complications for all the urgent DB-ERCP procedures were observed in 2 of the 30 procedures (6.7%), whereas complications for all the nonurgent procedures were 8 of the 114 procedures (7.0%). No procedure-related death was observed in urgent and nonurgent DB-ERCP.
**Conclusion:** Urgent DB-ERCP is an effective and safe treatment choice for patients with altered gastrointestinal anatomy who require acute biliary decompression.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0753 UTILITY OF SINGLE-BALLOON ENTEROSCOPY FOR THE DIAGNOSIS AND MANAGEMENT OF SMALL BOWEL POLYPS/TUMORS DETECTED IN CAPSULE ENDOSCOPY

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**Introduction:** Small-bowel polyps/tumors have been difficult to diagnose as a consequence of the poor accessibility to small bowel (SB). Since the introduction of capsule endoscopy (CE) and overtube-assisted enteroscopy, the number of SB polyps/tumors that are diagnosed has increased. Data regarding the performance of single-balloon enteroscopy (SBE) for the diagnosis and management of SB polyps/tumors detected in CE are scarce.
**Aims & Methods:** We aimed to evaluate the performance of SBE for the diagnosis and management of SB polyps/tumors detected in CE. Among all the SBE performed at our tertiary centre between 2010 and 2015, we analyzed those performed for evaluation of SB polyps/tumors detected in CE. SBE was performed using an oral or anal approach according to the CE results.
**Results:** From 244 procedures, 61 (25%) were performed for evaluation of SB polyps and tumors detected in CE. Twenty-five (41%) patients were male with a mean age of $53 \pm 16$ years; Forty (65.6%) procedures were performed using an oral approach. SBE detected 72% (44/61) of the lesions previously identified in CE. The distribution of the lesions was: 18% proximal jejunum, 25% middle jejunum, 16% distal jejunum, 14% proximal ileum, 7% medium ileum and 20% distal ileum. Histopathological results were: 10 adenomas, 8 hamartomas, 3

adenocarcinomas, 6 inflammatory polyps, 2 follicular lymphomas, 2 inflammatory fibroid polyps, 2 hyperplastic polyps, 1 carcinoid tumor, 1 metastasis of renal cell carcinoma, 3 xanthomas and 6 subepithelial lesions. Polyps/tumor size in CE was the only factor that significantly influenced diagnostic accuracy of SBE: 95% for lesions larger than 10 mm versus 62% for lesions smaller than 10 mm ($p = 0.006$). SBE directly influenced patient's management in 57% (39/61) of the cases.

**Conclusion:** SBE has a good accuracy (72%) for the diagnosis of SB polyps/tumors detected in CE. Diagnostic accuracy increased to 95% for lesions larger than 10 mm in CE. SBE directly influenced patient's management in 57% (39/61) of the cases.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0754 SMALL BOWEL REBLEEDING AFTER A SECOND ENDOSCOPIC TREATMENT IS EVEN HIGHER THAN AFTER THE FIRST ENDOSCOPIC TREATMENT IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING

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**Introduction:** In western countries, small-bowel vascular lesions (SBVL) represent the most frequent small-bowel finding in patients submitted to balloon-assisted enteroscopy (BAE) for obscure gastrointestinal bleeding (OGIB).[1] The global rebleeding rate of SBVL after a first endoscopic treatment session is 40%, and there is limited data regarding the efficacy of further endoscopic therapeutic sessions in the reduction of the rebleeding rate of SBVL.[2]

**Objective:** Evaluate the rebleeding rate of SBVL, after two endoscopic therapeutic sessions with BAE.

**Methods:** Between July 2007 and August 2015, all patients with rebleeding after a first endoscopic therapeutic session of SBVL who underwent a second BAE therapy session were included. The endpoint was a second episode of rebleeding, defined as the presence of overt OGIB, the need for red blood cells transfusions or a decrease in haemoglobin $\geq 2$ g/dL. Statistical analysis: Kaplan-Meier survival curves. Significance: $p < 0.05$.

**Results:** 17 patients with rebleeding SBVL after a first BAE therapy session were included, 52.9% (n = 9) were men with a median age of 71 years. In 94.1% (n = 16) patients, further endoscopic and/or radiologic exams were performed. A second BAE was performed in 70.6% (n = 12) patients, using an antegrade insertion in 75% (n = 9) of the cases and a retrograde insertion in 8.3% (n = 1) of the cases. The remaining two patients had a complete BAE. Angioectasias were identified in 83.3% (n = 10) of BAE, all classified as type 1 b in Yamamoto's classification.[3] Findings were multiple in 60% (n = 6) of the cases, with a median of 3.5 angioectasias per exam. Argon plasma coagulation was performed in all BAE with angioectasias (n = 10). Rebleeding occurred in 60% (n = 6) of patients after a second BAE therapeutic session, manifested as overt OGIB in 50% (n = 3), need of blood transfusion in 33.3% (n = 2) and haemoglobin drop $\geq 2$ g/dL in 16.7% (n = 1). The rebleeding rate at 1 year was 60%, and no further rebleeding was observed in the remaining period of follow-up.

**Conclusion:** Despite the high rebleeding rate detected shortly after endoscopic therapy, further endoscopic sessions of SBVL might be beneficial due to the relative effective reduction of rebleeding in a group of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0755 EFFECTS OF COMBINED CAPSULE AND BALLON-ASSISTED ENTEROSCOPY ON SURGICAL ACTIVITY FOR SMALL BOWEL DISEASES BASED ON 10-YEARS CLINICAL EXPERIENCE

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**Introduction:** The recent development of new enteroscopic modalities, such as video capsule endoscopy (VCE) and device-assisted enteroscopy, including balloon-assisted enteroscopy (BAE), has given the opportunity to evaluate the small bowel diseases and allows for the most accurate therapy. Suspected small bowel tumors and obscure bleeding was an often reason for the surgery.

**Aims & Methods:** The aim of the study is to evaluate the clinical utility of VCE and BAE in the clinical practice of the surgical hospital. From 14.02.2007 to 28.03.2016 enteroscopy was performed in 473 patients (m-247, f-226, mean age $47.9 \pm 16.9$ years, range 18–84), including 24 postoperative patients with long afferent loop for performing therapeutic ERCP. The indications for small bowel evaluation in 449 pts included: suspected small bowel bleeding – in 164 (36.5%) pts, small bowel tumor – in 88 (19.6%) pts, inflammatory bowel disease (IBD)-in 110 (24.5%) pts, others (carcinophobia, helminthosis, etc.) – in 87 (19.4%) pts. We performed 345 VCE in 328 (73.0%) pts. BAE was performed in 121 (26.9%) pts. Totally we performed 227 BAE by oral approach, including 26 repeated procedures in 11 pts; and 134 BAE by transanal approach, including 6 repeated procedures in 6 pts. Combination (VCE+ BAE) was performed in 133 (40.5%) of 328 pts.

**Results:** BAE was successfully performed in 443 (98.6%) of 449 pts. Using VCE and BAE we were able to reveal small bowel abnormalities – in 255 (57.6%) pts: vessel pathology in 60 (23.5%) pts, tumors in 74 (29.0%) pts, enteropathy – in 92 (36.1%) pts, other disorders – in 29 (11.4%) pts.; no abnormalities in 188 (42.4%) pts. Endoscopic treatment was performed in 63 (24.7%) pts, mostly including the removing of hamartomas in 14 (22.2%) patients with Peutz-Jeghers syndrome and endoscopic hemostasis in 26 (41.3%) patients with vessel pathology. Surgical treatment was performed in 41 (16.1%) pts, mostly because of the small bowel tumors. Capsule retention was the only adverse event, related to VCE, in 6 (1.8%) pts. Adverse events, related to BAE, were revealed in 6 (1.8%) pts: bleeding after biopsy (3), perforation (1) and gastric cardia tears (2).

**Conclusion:** VCE and BAE plays a significant role in the diagnosis and treatment of patients giving the opportunity to be treated endoscopically in 25.0% and to avoid surgery in 83.9% of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0756 A PROSPECTIVE 24-WEEK MUCOSAL HEALING AND DEEP REMISSION ASSESSMENT OF SMALL BOWEL AND COLONIC CROHN'S DISEASE AS DETECTED BY COLON CAPSULE ENDOSCOPY

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**Introduction:** Data on small bowel (SB) mucosal healing (MH) and deep remission (DR) in children with Crohn's disease (CD) are rare. Recently, colon capsule endoscopy (CCE) has been proved effective as "pan-endoscopy" in pediatric CD. This is the first study to prospectively assess MH and DR on the entire GI tract by performing two subsequent CCE over 24 weeks in children with CD in comparison with biomarkers, magnetic resonance enterography (MRE) and SB contrast ultrasonography (SICUS).

**Aims & Methods:** Children with known CD were prospectively recruited and underwent imaging studies followed by CCE, at baseline and after 24 weeks. The Lewis score (LS) and Simple endoscopic score for Crohn's disease (SES-CD) were calculated for SB and colon, respectively. C-reactive protein (CRP) and fecal calprotectin (FC) were also evaluated for their association with clinical activity, imaging and CCE findings. Clinical remission was defined as PCDAI < 10. SB and colonic MH were defined as LS < 135 and SES-CD $\leq 1$, respectively; moderate-to-severe inflammation was defined as LS > 790 or SES-CD > 7. Biomarker remission (BR) was defined as a combination of clinical remission (PCDAI < 10) and normal biomarkers. Deep remission (DR) was defined as a combination of BR and MH. Therapy was calibrated according to CCE results.

**Results:** Forty-eight patients (pts) were recruited, 22 with clinical and biomarker activity and 26 in remission. At baseline CCE confirmed significant inflammation (either in SB or colon) in 18 (82%) of 22 pts with clinical and/or biomarker disease activity, while showed mild lesions and/or normal mucosa in 4 (18%). MRE and SICUS did not demonstrate active disease in 5/18 (23%) with lesions at CCE, but it found nonspecific findings in 2 of 4 with negative CCE. Biomarker levels were elevated with FC in 13 (59%); CRP levels in 10 (45%) and either biomarker in 15 (68%). In the 26 pts with remission, CCE showed SB lesions in 13 (50%) and colonic lesions in 6 (23%). Complete MH and DR were observed in 10 (39%). Imaging studies found lesions only in 7 (27%, $p < 0.05$). At 24-week follow-up, CCE identified DR only in 8/20 (36%) of the active group; while in 12/20 (54%) showed a partial MH. In inactive pts, CCE revealed that only 7/10 pts maintained DR. Of 16 pts in remission and with lesions at baseline, CCE showed that 9 (56%) achieved DR and 5 (44%) a partial MH after a change of therapy. MRE and SICUS had a good concordance in evaluating DR (14/17, 82%) in both groups, but did not identify partial MH (only 8/17, 47%, $p < 0.05$). FC and CRP were not able to accurately evaluate DR in either group.

**Conclusion:** This study shows for the first time that CCE is effective for monitoring DR and MH of the entire GI tract and in directing therapy for pediatric patients with CD.

**Disclosure of Interest:** S. Oliva: I gave a lecture for Medtronic at last ECCO congress.
C. Hassan: Consultant for Medtronic
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All other authors have declared no conflicts of interest.

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## P0757 WHICH FACTORS MAY PREDICT THE FAILURE OF A COMPLETE SMALL-BOWEL EXAMINATION IN CAPSULE ENTEROSCOPY?


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Introduction

**Introduction/Objectives:** Capsule enteroscopy (CE) represents a valuable tool in the examination of small-bowel, with a higher diagnostic yield compared to radiology and angiography.[1] Nevertheless, the inability of reaching the cecum during the recording time of CE, prevents complete small-bowel assessment which negatively affects its diagnostic yield. Previous studies report that 15–33% of CE are incomplete.[2,3] Therefore, the identification of factors associated with incomplete CE is crucial. The aim of this study was to evaluate predictive factors associated with incomplete CE.

**Methods:** Between June 2009 and February 2016, all patients with incomplete small-bowel examination in CE (Mirocam®) were included. This case group was compared with a control group which consisted of all patients with complete CE examinations submitted to CE between January 2014 and February 2016. Patients with an ileostomy, retained CE and CE directly placed in the duodenum were excluded. Data regarding demography, degree of dependency of patients, past medical and surgical history, medications, CE parameters and its regimen of performance (inpatient/outpatient regimen) was analyzed. Statistical analysis: $X^2$, Student's t-test and binary logistic regression. Significance: $p < 0.05$.

**Results:** One hundred and fifty-three patients were included, 31 cases and 122 controls. Among the parameters analysed, factors significantly associated with incomplete CE included inpatient regimen ($p < 0.0001$), prior abdominal surgery ($p = 0.019$), higher degrees of dependency ($p = 0.008$) and opiate use ($p = 0.019$). In logistic regression, the degree of dependency ($OR = 4.67$; $p = 0.028$), performance of CE in hospitalized patients ($OR = 4.04$; $p = 0.006$) and prior abdominal surgery ($OR = 3.45$; $p = 0.012$) represented the independent predictive factors of an incomplete CE.

**Conclusion:** Patients hospitalized and with higher degrees of dependency and prior abdominal surgeries are more likely to have an incomplete assessment of small-bowel in CE. The recognition of these factors may contribute to the adoption of specific measures to decrease the rate of incomplete exams.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0758 IMMEDIATE DUODENAL DELEVERY, VS DELAYED ORAL INGESTION, OF CAPSULE ENDOSCOPY: IS THE SOONER THE BETTER? A PROSPECTIVE COMPARISON OF SMALL BOWEL VISUALIZATION QUALITY, ACCORDING TO A COMPUTED ASSESSMENT OF CLEANSING SCORE


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**Introduction:** The early timing of the Small Bowel (SB) Capsule Endoscopy (CE) is an independent predictor of positive findings in Obscure GastroIntestinal Bleeding (OGIB). Duodenal delivery of SBCE immediately after normal gastroscopy and colonoscopy may enable significant time savings, and therefore increase the diagnosis yield. However, the quality of SB visualization after immediate duodenal delivery is not known.

**Aims & Methods:** Our aim was to compare the quality of SB visualization after immediate duodenal delivery to the standard procedure (postponed SBCE ingestion after oral preparation). This was a prospective case-control study. After sample size calculation, 48 patients with OGIB were selected. Patients with active hemorrhage on SBCE were excluded, as bowel visualization would likely be altered downstream the bleeding site. Twenty-two cases (group 1) were included and matched to 22 controls (group 2) according to gender, age and type of bleeding (patent/occult). Patients in group 1 received a split 4 L PEG preparation before SBCE was delivered into the duodenum immediately after normal colonoscopy. Patients in group 2 received 1 L of PEG the day before ingesting the SBCE, distant from the initial bidirectional endoscopies. A validated Computed Assessment of Cleansing (CAC) score, based on the automated calculation of the ratio of red and green pixels (R/V) of each frame of each video sequence of the SB, was used for objective comparison.

**Results:** A preliminary study confirmed good correlations between reddish frames (with $CAC > 1.6$) and those deemed adequately cleansed by 2 blinded expert readers. The average time intervals between admission for OGIB and delivered or delayed SBCE, were 4 days for overt bleeding, and 65 days for occult bleeding. The proportions of "adequately cleansed" frames according to the CAC did not differ significantly between the 2 groups ($p = 0.28$). There was no significant difference between the 2 groups terms of SB transit time ($p = 0.53$), total number of SB frames ($p = 0.21$), and rates of complete SB examination.

| | Group 1 (delivery) n = 22 | Groupe 2 (ingestion) n = 22 | p |
|---|---|---|---|
| **Proportion of adequatelycleansed frames (CAC ≥ 1.6)** | | | |
| Over the entire sequence | 43.1% | 50.0% | 0.28 |
| Within the 1st quartile | 57.4% | 59.2% | 0.86 |
| Within the 2nd quartile | 46.6% | 49.9% | 0.88 |
| Within the 3rd quartile | 38.7% | 47.2% | 0.47 |
| Within the 4th quartile | 31.9% | 41.1% | 0.42 |
| **Secondary outcomes** | | | |
| Complete examination of the small bowel: n (%) | 22 (100%) | 21 (95.5%) | ns |
| Mean number of small bowel frames | 12451 | 13800 | 0.21 |
| Mean transit time (minutes) | 267 | 273 | 0.53 |

**Conclusion:** According to an objective CAC score, SBCE delivery into the duodenum in OGIB, immediately after normal bidirectional endoscopies, allows a SB quality of visualization not different to that of the delayed standard procedure, with virtualy no delay and no additionnal preparation for patients. The potential of this approach to increase the diagnostic yield of SBCE in OGID, and to decrease the length of hospital staying, should be evaluated.

**Disclosure of Interest:** X. Dray: Xavier Dray has received lecture fees from Given/Covidien/Medtronics

All other authors have declared no conflicts of interest.


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## P0759 IS THERE ROLE OF PRE-READER FOR EXPERT, IN REAL CLINICAL FIELD OF VIDEO CAPSULE ENDOSCOPY INTERPRETATION


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**Introduction:** Capsule endoscopy (CE) has become an important tool for the diagnosis of small bowel disease. A major problem of CE is that it is time consuming to read one case. Although few previous studies have showed a supporting role of Pre-Reader in the reading of CE, it remains controversial. In this study, we aimed to show the complement role of low experienced endoscopy trainee (VCE < 20) in the interpretation of CE.

**Aims & Methods:** Before the study, pre-readers was educated about RAPID® for PillCam Software. The 50 educational cases (which including 12 vascular lesions, 21 ulcerative lesions, and 16 neoplastic lesions) were selected from our

hospital. Two Endoscopy trainees, as a pre-reader, interpretated 50 cases of CE and completed the assessment form. After that, highly experienced endoscopists (VCE > 100) reviewed each case individually with reference to the filled out assessment form. Same videos, which didn't include the Pre-Readers assessment form were reviewed by another high experienced endoscopists too. We evaluated the agreement, missed lesion, overcalled, and reading time between two expert groups.
**Results:** At assessment form, which filled up by Pre-reader, agreement (A)/missed lesion(M)/overcalled(O) were observed in 72.3%/ 8.9%/18.8% respectively. The agreement rate was high in vascular and ulcerative lesions, On the other hand, overcalled lesion was high in neoplastic, especially polypoid lesion. Pre-reader's assessment form supported experts to get more abnormal findings (detection rate was improved by 10~20%), however final diagnosis was not changed. Pre-reader's assessment form added more information as well as decreased expert's time significantly.
**Conclusion:** Pre-reader added more information on capsule endoscopy, even though the final diagnosis was not changed. Also, a group of pre-readers could decrease the time spent. In this study, we showed complement role of pre-reader in the reading of CE.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0760 IS FECAL CALPROTECTIN A SENSITIVE BIOMARKER FOR SMALL BOWEL CROHN'S DISEASE AS DETECTED BY CAPSULE ENDOSCOPY?

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**Introduction:** Small bowel capsule endoscopy (SBCE) is a useful diagnostic tool for small bowel Crohn's disease (CD), with a higher diagnostic yield than standard radiological techniques. However, the majority of patients undergoing either modality do not have CD. As with standard endoscopy a tool to help select patients with probable IBD would be clinically useful.
**Aims & Methods:** To correlate a single Fecal calprotectin (FC) concentration with SBCE findings in patients with suspected or known small bowel CD. In this prospective study patients with suspected or known CD scheduled to have a SBCE were requested to give a stool sample for fecal calprotectin (FC) on the day of examination. In addition to FC, CRP (normal < 5 mg/L) and Harvey Bradshaw index (< 5 is normal) was calculated. SBCE was performed as standard and read by experienced gastroenterologists. A SBCE with a Lewis score of >135 or >3 significant ulcers was considered positive for CD. FC was analyzed externally and results reported as ug/g stool. The predictive value of a FC > 50ug/g and 100ug/g for CD was calculated and overall correlation assessed with pearsons r.
**Results:** To date 84 patients have been invited to participate and 53/84(63%) have both a FC and SBCE results available at the time of analysis of which; male = 22 (38%), established CD (n = 5), suspected CD (n = 48), median age was 47yrs (range 17 to 75), median CRP was 1.55 mg/L (range 1 to 28.2) and median FC was 53ug/g (range 19.5 to 774). In all 47% (25/53) had a normal FC <50ug/g, and 35% (19/53) FC > 90 (median 217; range 102.8 to 774) and 9 an indeterminate FC >50 and< 90. Overall 12/53 (22.6%) had a positive SBCE for Crohn's disease. Overall FC was weakly correlated with SBCE, with pearsons's r of 0.4401. The sensitivity, specificity and positive and negative predictive values for FC cut off's of >50ug/g and >100ug/g were; FC >50ug/g 67%, 53%, 31% and 83% and FC >100 ug/g 58%, 71%, 39% and 84%. The sensitivity, specificity and PPV and NPV for a CRP cut off >5 mg/L was; sensitivity 27%, specificity 86%, PPV 37%, NPV 78%. Similarly neither HBI nor CRP correlated with SBCE findings.
**Conclusion:** In our prospective study FC weakly correlated with SBCE findings in both suspected and known CD patients. This may reflect the lack of colonic disease in the majority of our patients. However a FC of <100 ug/g has an adequate NPV at 84%, which was higher than for CRP and may be useful clinically and warrants further investigation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0761 FECAL CALPROTECTIN AS A SELECTION TOOL FOR SMALL BOWEL CAPSULE ENDOSCOPY IN SUSPECTED CROHN'S DISEASE

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**Introduction:** The small bowel capsule endoscopy (SBCE) is a first-line method in patients with suspected Crohn's disease (CD) after a previous negative ileocolonoscopy. Fecal calprotectin (FC) is a non-invasive marker of intestinal inflammation and has demonstrated an excellent diagnostic accuracy in distinguishing inflammatory bowel disease and functional disease.
**Aims & Methods:** The aim of this study was to evaluate the predictive value of the FC in inflammatory activity detected by SBCE in patients with suspected CD and negative ileocolonoscopy. Retrospective study included patients who underwent SBCE for suspected CD between March 2015 and March 2016. FC was measured within one week of SBCE. Inflammatory activity was considered significant when the Lewis score (LS) ≥135. FC was correlated with LS using Spearman correlation. The diagnostic accuracy of FC for significant activity was calculated by area under the curve (AUC).
**Results:** Fifty-five patients were included: 38 females (69.1%), mean age of 38 years. The FC was correlated positively and significantly to LS ($rs = 0.571$, $p < 0.001$). The SBCE detected significant inflammatory activity (LS ≥135) in 27 patients (49.1%). The AUC of FC was 0.864 for significant inflammatory activity (LS ≥135). For values of FC≥100 µg/g, a LS≥135 was found in 22 patients (40%), $p < 0.001$, corresponding to a sensitivity, specificity, positive predictive value and negative predictive value of 81.5%, 85.7%, 84.6% and 82.8%, respectively.
**Conclusion:** The FC has shown a good ability to predict significant inflammatory activity in SBCE in patients with suspected CD. Thus, the FC proved to be a useful tool to select patients with suspected CD for SBCE.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0762 USEFULNESS OF THE NEWLY DESIGNED PLASTIC STENT FOR EUS-GUIDED HEPATICOGASTROSTOMY AND PANCREATIC DUCT DRAINAGE: LARGE CASE SERIES EVALUATION

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**Introduction:** Recently, EUS-guided biliary and pancreatic duct drainage has emerged in case of failed ERCP. Apart from established ERCP, there are several obstacles to perform successful drainages. The most big issue is few dedicated EUS-guided devices for EUS-biliary and pancreatic duct drainage. Thus, we developed a new single pigtail plastic stent designed for EUS-guided interventions (EUS-guided hepaticogastrostomy;EUS-HGS and pancreatic duct drainage;EUS-PD) and used as the first-line EUS-guided stent until now.
**Aims & Methods:** The aim of this study is to retrospectively evaluate the feasibility and efficacy of newly designed plastic stent. Thirty-two patients with biliary obstruction due to benign or malignant biliary strictures or common bile duct stones underwent EUS-HGS. And Twenty-two patients with acute recurrent pancreatitis due to main pancreatic duct stricture or stenotic pancreatojejunostomy underwent EUS-PD. Totally a new plastic stent was used in fifty-four patients. EUS-PD and HGS were performed using a 19-gauge or 22-gauge fine-needle. When bile duct dilatation is insufficient, it is possible to use a 0.021-inch guidewire with a 22 G needle. Dilation of the needle tract and anastomotic site was performed by using a standard or tapered catheter, a cautery dilator, an 8F dilation catheter. After tract dilation, new tapered tip and four-fold-flanged single pigtail plastic stent (8F for EUS-HGS, 7F for EUS-PD, total length: 20-cm, effective length: 15-cm, flanges: 4 with apertures, side holes: total 12 holes, distal straight site, 4 holes and pigtail site, 8 holes) was placed.
**Results:** New plastic stent was placed successfully without procedural complication in all cases (54/54, 100%). Treatment success rate was 96.9% (31/32) in EUS-HGS and 100% (22/22) in EUS-PD. In EUS-HGS, bleeding from the punctured gastric wall occurred in one patient three days postoperatively. We exchanged the plastic stent for a fully covered self-expandable metal stent (8 mm in diameter). Hemostasis was achieved and rebleeding did not occur. A mild adverse event of self-limited abdominal pain occurred in three patients. There was no stent migration or dislocation. In EUS-PD, self-limited abdominal pain was observed in three patients, bleeding in one patient one day postoperatively (interventional radiology and transcatheter arterial embolization were needed), and mild pancreatitis in one patient, but there were no stent migration.
**Conclusion:** We designed a new single-pigtail plastic stent dedicated for EUS-guided interventions (EUS-HGS and EUS-PD) and confirmed its technical feasibility and clinical effectiveness. Additional long-term studies involving a sufficient number of patients are warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0763 A NOVEL LUMEN-APPOSING METAL STENT FOR ENDOSCOPIC ULTRASOUND-GUIDED DRAINAGE: A SINGLE CENTER EXPERIENCE

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**Introduction:** Recently Lumen-apposing metal stent (LAMS) specifically designed for interventional EUS (Hot-AXIOS$^{TM}$), had significantly changed the technical approach in the setting of EUS-guided drainage.
**Aims & Methods:** The aim of this study was to evaluate the feasibility, safety and efficacy of the Hot-AXIOS$^{TM}$ stent placement in different clinical setting in a tertiary referral center. The Hot-AXIOS stent (Boston Scientific) is a fully covered, nitinol, braided stent with bilateral anchor flanges. We prospectively gathered data from consecutive patients treated with this device between March 2014 and April 2016. Clinical applications are various including pancreatic fluid collection, gallbladder and biliary drainage. Technical success was defined as correct positioning of stent. Clinical success was defined as complete resolution of the pancreatic collection and of the patient's symptoms in pancreatic pseudocyst drainage; radiologic evidence of gallbladder decompression and resolution of clinical symptoms in cholecystitis; serum bilirubin level decreased by 50% or more within 2 weeks after the procedure in biliary drainage.
**Results:** Thirty-nine patients were treated with LAMS (Hot-AXIOS) stent placement. Population cohort was composed of 16 male and 23 female, with mean age of 68.7 years (ranging from 37–95 y). The indication of EUS drainage were: 18 (46.2%) pancreatic collections (2 pancreatic necrosis), 10 (25.6%) acute cholecystitis in patients not fit for surgery, 11 (28.2%) biliary drainage in patient with pancreatic or duodenal neoplasm and papilla of Vater unreachable by ERCP. All stents were successfully positioned. Twenty-six stents were placed transgastric, 13 transduodenal. The stent diameter was 6 mm in 5 patients, 8 mm in 3 patients, 10 mm in 14 patients and 15 in the remaining 17 patients. All patients were treated under deep sedation with propofol, with the linear array Olympus GF-UCT-180 series echoendoscopes, in a single step fluoroless procedure. The mean duration of EUS interventional procedure was 22.3 minutes (ranging for 7 to 50). Three (7.7%) adverse events were observed (one self-limited intra-procedural bleeding during gallbladder drainage and two late re-infections of necrosis in pancreatic collection drainage). There were no major complication. The mean duration of time for stent placement was 3.2 minutes (ranging for 1 to 15). Stent removal was safely performed in 9 out 18 patients treated for PFC, after a median of 3.8 months. No complications occurred during stent removal. Biliary and gallbladder stent were permanently positioned and therefore were not removed. Clinical success was observed in all patients.
**Conclusion:** To the best of our knowledge, this is the first comprehensive analysis of feasibility, safety and efficacy of EUS-guided drainages with new lumen-apposing metal stent (Hot-AXIOS$^{TM}$ system) for multiple indications. Up to now, transmural drainages were performed with devices borrowed from ERCO and not specifically designed for interventional EUS. The availability of new devices, such as Hot-AXIOS$^{TM}$, developed for interventional EUS could significantly change the technical approach of these procedures, allowing an easier, quicker and safer procedures with high technical and clinical success rates. Our results will have to be confirmed by multicenter controlled studies with large populations.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0764 LONG-TERM OUTCOMES OF A NEWLY DEVELOPED HYBRID METAL STENT FOR ENDOSCOPIC ULTRASOUND–GUIDED BILIARY DRAINAGE

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**Introduction:** Endoscopic ultrasound–guided biliary drainage (EUS-BD) has been proposed as an alternative in patients whom endoscopic retrograde cholangiopancreatography (ERCP) has failed. Although a fully covered self-expandable metal stent (FCSEMS) has been commonly used for EUS-BD, but migration of the FCSEMS is one of the main limitations of this procedure.
**Aims & Methods:** In the present study, we evaluated the technical and clinical success rate, adverse events and long-term outcomes of the newly developed hybrid stents customized for EUS-BD. From September 2011 to May 2015, a total of 54 consecutive patients with biliary obstruction who were candidates for an alternative technique for biliary drainage because of failed ERCP were enrolled. We conducted a prospective observational study.
**Results:** EUS-guided hepaticogastrostomy (EUS-HGS) was performed in 21 patients, and EUS-guided choledochoduodenostomy (EUS-CDS) was performed in 33 patients. The technical success rate of EUS-BD was 100% (54/54), while the clinical success rate was 94.4% (51/54). Immediate adverse events developed after EUS-BD in 9 patients (16.6%; cholangitis (n = 3), bleeding (n = 2), self-limited pneumoperitoneum (n = 3), and abdominal pain (n = 1)). During the follow-up period (median 143, IQR: 80–239 days), proximal or distal stent migration was not observed, and the mean stent patency duration was 166.3 days in EUS-HGS and 329.1 days in EUS-CDS group, respectively.
**Conclusion:** EUS-BD with the hybrid metal stent is technically feasible and can be an effective treatment for biliary obstruction after failed ERCP. Hybrid metal stents may be used safely in EUS-BD and it can reduce stent-related adverse events, especially stent migrations.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0765 THE ACTUAL IMPACT OF PREOPERATIVE BILIARY DRAINAGE ON POSTOPERATIVE OUTCOME: ANALYSIS OF 1000 CONSECUTIVE PANCREATICODUODENECTOMIES

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**Introduction:** Patients with periampullary neoplasms frequently present with obstructive jaundice. Bile obstruction may lead to hepatic dysfunction, coagulation disorders, cholangitis and hepatotoxicity. In the attempt to palliate symptoms and systemic disorders associated with hyperbilirubinemia, a preoperative biliary drain (PBD) is often performed. Several studies have revealed that PBD decreases postoperative mortality and morbidity rates compared to jaundiced patients. However, other studies argued that PBD increases surgical site infection, major surgical complications and mortality rates. Although PBD has been routinely conducted to ensure safe anesthesia and operation, the beneficial effects of PBD remain uncertain. In addition, even when PBD is performed, the selection of either a plastic or a metal stent remains controversial and its prognostic impact on long-term survival is still unknown.
**Aims & Methods:** The aim of this study was to examine the impact of preoperative jaundice and PBD on complications following pancreaticoduodenectomy (PD). We retrospectively analyzed 1000 consecutive patients who underwent PD at our Institution from 2005 to 2014. The population was divided into three groups based on PBD (SG), preoperative jaundice without PBD (JG) and control group (CG).
**Results:** The overall postoperative morbidity and mortality were 60% and 1.9%, respectively. A comparison among the three groups and within CG and SG showed a significantly higher morbidity rate in SG ($p = 0.019$;OR 1.2 and $p = 0.007$;OR 1.2, respectively). No difference was found in the mortality rate. Overall, major complications (Clavien-Dindo $\geq$ III) occurred in 22.7% of patients, with a significantly higher rate in SG (compared to CG, $p = 0.010$; OR 0.8). Abdominal abscess, sepsis and wound infection were found significantly higher in SG ($p < 0.05$). Within the JG a preoperative bilirubin cut-off value of 4 mg/dl seems to predict a worse postoperative outcome: morbidity rate ($p = 0.027$ OR 1.9), grade C fistula ($p = 0.011$ OR 0.8), length of stay ($p = 0.032$ OR 1.0) and reoperation ($p = 0.002$ OR 5.5) rates were significantly higher with preoperative levels greater than 4 mg/dl. There was no significant difference on morbidity and mortality rates in SG and JG patients with Bilirubin levels $\geq$ 4 mg/dl, however the latters showed a higher rate of reoperations ($p < 0.001$ OR 1.5).
**Conclusion:** Obstructive jaundice is one of the commonest symptoms in patients with periampullary tumors. Despite theoretical advantages, the use of PBD remains controversial because it has failed to show an actual clinical benefit, suggesting, on the contrary, an adverse impact on perioperative outcome. Our study demonstrates that stented patients have higher morbidity rate and major complications than controls. Instead, there was not significant difference in morbidity, major complications, and mortality rates between JG and SG. We showed that the PBD does not increase major complications in PD, but resulted in a significant increase in the risk of postoperative infectious complications and wound infections. We also confirm previous findings that a preoperative bilirubin cut-off value of 4 mg/dl in non-stented patients seems to best predict postoperative outcome. We did not find differences between SG and JG patients with Bilirubin levels $\geq$4 mg/dl in morbidity and mortality rates, major complications and lenght of stay between the groups. However, there was a statically significant difference in wound infection and reoperation rate. PBD is associated with infectious complications, so we propose that intraoperative bile cultures should be routinely obtained during PD to tailor antibiotic therapy in case of infectious complications. Patients with preoperative Bilirubin levels $\geq$4 mg/dl should be evaluated for a PBD in order to reduce the complications related to jaundice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0766 WIRELESS EUS-GUIDED CHOLEDOCHODUODENOSTOMY BY A CAUTERY-TIPPED LUMEN APPOSING METAL STENT FOLLOWED BY DUODENAL METAL STENT PLACEMENT: A SINGLE SESSION SEQUENTIAL APPROACH FOR CONCOMITANT MALIGNANT BILIARY AND DUODENAL OBSTRUCTION

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**Introduction:** In patients with distal malignant biliary obstruction and concomitant duodenal obstruction, biliary endoscopic palliation can be obtained by EUS-guided biliary drainage either before or after duodenal stent placement. Novel cautery-tipped lumen apposing metal stent (LAMS) have been recently developed for this purpose.
**Aim**: We evaluate the technical success and clinical efficacy of EUS-guided biliary drainage and duodenal stenting performed in a single session in patients with unreachable papilla due to malignant duodenal obstruction.
**Methods**: Retrospective analysis of a prospectively maintained data base aimed to evaluate the technical success (defined as correct positioning of the stent) of the new single session approach. We included 5 consecutive patients referred for malignancy involving both the duodenum and the bile duct. Four were affected by unresectable pancreatic cancer (3M/1 F, mean age 63.8 y) and one by duodenal adenocarcinoma (1 M, 53 y) referred for endoscopic palliation.
**Results:** All the patients were treated with a new single session sequential approach by deployment of LAMS and duodenal stent after failed ERCP. During procedures, patients were deeply sedated with propofol under and carbon dioxide insufflation was used. The linear array Olympus GF-UCT-180 series echoendoscopes at 5–10 MHz in combination with the echoprocessor EU-ME2 were used. Under EUS-guidance, the biliary duct was punctured from the duodenal bulb and hot-axios stent was deployed in a fuoroless and wireless manner. Afterward, the duodenal stent was placed under fluoroscopic during the same section. The procedures were well tolerated; the whole mean procedural time was $45 \pm 5.7$ min (range 38–52 min) and $19 \pm 0.8$ min (range 18–20) for EUS-CDS. All patients had clinical resolution of their jaundice within the first week and started their oral intake the day after the procedure. Overall technical success rate for both EUS-guided choledochoduodenostomy and duodenal stenting was 100%. There were no procedure-related adverse events. Clinical success rate was 100% with mean follow up of 3 months (SD 1.3 m).
**Conclusion:** When a transpapillary biliary drainage is not feasible, EUS-CDS may provide an alternative biliary drainage route away from both duodenal and biliary obstruction. The introduction of specific stent designed for transluminal endoscopic intervention such as LAMS minimizes the risk of bile leakage and stent migration and makes the transmural approach potentially more effective and safe. Single session approach for biliary and duodenal obstruction palliation, using cautery-assisted LAMS, could be proposed as safely and effectively technique in patients with unreachable papilla due to malignant obstruction.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0767 EUS-ASSISTED CHOLEDOCHODUODENOSTOMY WITH METAL STENTS FOR PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION: A COMPARATIVE ANALYSIS OF OUTCOMES BETWEEN TUBULAR AND LUMEN-APPOSING STENTS

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**Introduction:** EUS-guided biliary drainage with tubular (plastic or metal) stents is the standard approach for patients with malignant biliary obstruction (MBO) unfit for surgery after failed or unfeasible ERCP. Choledochoduodenostomy (CD) with tubular self-expanding metal stents (tSEMS) have some drawbacks such as migration, shortening, bile leakage or cholecystitis secondary to blockade of cystic duct: all of them could be prevented by means of lumen-apposing metal stents (LAMS). However, LAMS insertion in this setting is technically demanding because of angulation of echoendoscope tip at duodenal bulb and the narrow caliber of biliary lumen. We aimed at comparing efectiveness, safety and technical feasibility between both techniques in a consecutive series of MBO patients.
**Aims & Methods:** Retrospective review of a prospectively maIntained database including all MBO patients who underwent EUS-guided choledochoduodenostomy. Patients receiving full-covered tSEMS (10 x 60 mm) were matched with those drained with LAMS (AXIOS$^{TM}$, Xlumena, CA, USA: 10 x 10 mm & 6 x 8 mm; conventional 'cold' and electrocautery-equipped -'hot'- LAMS) and compared according to sex, age, ASA score, etiology,overall survival time, technical & clinical success and rate of adverse events. Technical success: Stent deployment in the correct position. Clinical success: decrease in bilirubin concentration to less than 50% of the preprocedure values. Statistical analysis was carried using SPSS v 17.0 and results compared by Student's t test for continuos variables and $\chi^2$ test/ Fisher's exact test for categorical variables. P values $\leq 0.05$ were considered significant.
**Results:** 25 patients were included: tSEMS vs LAMS = 13: 12. LAMS Ø 6 mm / 10 mm: 10/2 pts, Hot-LAMS: 6 pts. Inclusion period: tSEMS: Oct'10–Nov'14; LAMS: March'12–Nov'15. Mean follow-up (days): tSEMS/LAMS: 138.2 (20–283) / 116.5 (6–342). No differences were observed with regard to age, sex, ASA score, overall survival time and etiology of malignance. There were neither significant differences tSEMS/LAMS referred to: 1.-Technical success rate: 12/13 (92.30%) vs 11/12 (91.66%); $p = 0.25$, 2.- Clinical success: 11/13 (84.61%) vs 10/12 (83.33%); $p = 0.19$, 3.-Adverse events :2/13 (15.38%) vs 2/12 (16.6%) $p = 0.116$. Adverse events: tSEMS: Early: Biliary duct perforation. Late: acute cholecystitis. LAMS: Early: scant biliay leak, dislodgement of distal flange with rescue by coaxial insertion of a plastic stent. There were no clinical data of stent dysfunction in either group.
**Conclusion:** EUS-guided CD with LAMS appears to provide a highly safe and effective procedure with quite similar results than tSEMS for drainage of malignant biliary obstruction. Further larger, prospective and randomized studies are needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0768 EFFICACY AND SAFETY OF ENDOSCOPIC-ULTRASOUND GUIDED BILIARY DRAINAGE; AN UPDATE META-ANALYSIS

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**Introduction:** Success and event rate of EUS-guided biliary drainage varies with techniques and results from different studies remain inconsistent. We conducted a proportion meta-analysis to evaluate efficacy and safety of EUS-guided biliary drainage and to compare the different procedures and biliary access route.
**Aims & Methods:** We searched MEDLINE, EMBASE,COCHRANE and SCOPUS to identify studies reporting technical success, clinical success and complcation rate of EUS-guided biliary drainage technique with a sample size greater than 5 patients. Weighted pooled rate and 95% confident interval were calculated to estimate clinical effectiveness and safety of EUS-guided biliary drainage procedure.
**Results:** We identified 49 studies with a total of 885 patients (371 choledocho-duodenostomies, 249 hepaticogastrostomies and 336 rendez-vous technique). The overall technical success rate, clinical success rate and complications rate with 95% confidence interval were 88% (83%–91%), 92% (89–94%) and 21% (18–25%) respectively with no publication bias ($p = 0.326$, $p = 0.903$ and $p = 0.203$ respectively). There was no difference in technical and clinical success rate using either intra-hepatic or extra-hepatic approach (OR = 0.98[0.93–1.03] and OR = 0.99[0.90–1.09] respectively).
**Conclusion:** EUS-guided biliary drainage appears to be an effective treatment when ERCP fails with a high success rate and acceptable adverse event rate. There was no significant difference between the intra-hepatic or extra-hepatic approaches. Prospective randomized controlled studies are required to further evaluate the difference between the 2 approaches.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0769 NEWLY DEVELOPED FLOWER-TYPE COVERED SELF-EXPANDABLE METAL STENT FOR PREVENTING CHOLECYSTITIS AND PANCREATITIS: PHYSICAL PROPERTIES

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**Introduction:** The conventional, cylindrical fully covered self expandable metallic stent (C-CSEMS) has its limitations with high risks of blocking the cystic duct, and the branches of pancreatic ducts in accordance with the stent design and the properties of the covered materials. The need for a new stent design was indispensable, such as a flower type, five-petal shaped design with side grooves, fully covered self-expandable metallic stent (F-CSEMS).
**Aims & Methods:** A comparison study regarding the experimental results for the physical properties accomplished with a conventional e-PTFE covered self-expandable metallic stent (C-CSEMS) and the newly developed flower-type e-PTFE covered self-expandable metallic stent (F-CSEMS). The physical experimental study was performed in between the conventional cylindrical type covered stent and the newly developed flower-type covered stent with the same specification of 8 mm in diameter, 12.5 cm in length, e-PTFE covered material with the cell size of the 2 mm. The main comparison was based on the following factors: flexibility using banding test, shortening rate by loading the stent into the 8Fr. Delivery system and the drainage rate by measuring drained amount of water in 5 minutes.
**Results:** The flexibility was measured through the bending test and the result for F-CSEMS was 0.41 N where as the C-CSEMS was 0.65 N. The fact that F-CSEMS has more flexibility as compared to the C-CSEMS has been proven since the less force it needs for banding the better flexibility it gives. As per the shortening rate, the F-CSEMS stent with the length of 12.5 cm has been loaded into the 8Fr. Delivery system and the final length inside the delivery system was measured as 15 cm. The same length of C-CSEMS has been loaded into the same

8Fr. Delivery system and the final length was approximately 17.9 cm. Therefore, the shortening rate for F-CSEMS was determined as low as 20% where as the C-CSEMS was determined as 30%. The drainage test was performed by draining water outside the stent in a cylindrical tube with the 8 mm of inner diameter and measuring the amount of water that it got drained in 5 minutes. The F-CSEMS drained 100 ml of water through the grooves on the outside of the stent where as the C-CSEMS could not drain anything at all for the whole time.
**Conclusion:** The newly developed flower-type covered self-expandable metal stent has been proved to have more flexibility with less shortening rate of 20% as well as the full drainage of liquid through the special grooves formed outside of the stent design. The animal test has been already done in 2014 and the clinical test will be needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0770 RISK FACTORS FOR POSTPROCEDURAL PANCREATITIS AFTER ENDOSCOPIC PAPILLECTOMY

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**Introduction:** Endoscopic papillectomy (EP) is increasingly used as an alternative to surgery for ampullary adenomas and other noninvasive lesions. However, it remains controversial as to which factors were associated with post-papillectomy pancreatitis.
**Aims & Methods:** The aim of this study is to analyze the rates of complications after EP, with a particular emphasis on risk factors associated with pancreatitis, especially endoscopic pancreatic sphincterotomy (EPS) and pancreatic stent insertion. We conducted a retrospective cohort study of all patients who underwent attempted endoscopic papillectomy for known or suspected ampullary tumors between July 2003 and March 2016. Through reviewing procedure reports and medical records, variables for patients and procedures were compared between cases with and without pancreatitis.
**Results:** Endoscopic papillectomy was performed in 93 patients with histological findings of low-grade dysplasia (41.9%), high-grade dysplasia (19.3%), carcinoma (22.6%), and others (18.3%). The rate of post-papillectomy pancreatitis was 10.7% (10/93). In this study, we compared with the categories, no additional procedure versus EPS and no additional procedure versus pancreatic stent insertion and EPS versus pancreatic stent insertion. There was no statistically significant difference in incidence rate of pancreatitis among those three groups, indicating no difference for each method to prevent the complication post-papillectomy pancreatitis ($P = 0.068$) In addition, age, sex, pathologic size, comorbidity, and the resection type were not statistically associated with post-papillectomy pancreatitis.
**Conclusion:** After papillectomy, pancreatic stent insertion ofwith endoscopic pancreatic sphincterotomy may not be effective to prevent post-papillectomy pancreatitis. Further prospective study is needed to confirm this result.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0771 OUTCOMES AND TECHNICAL METHODS OF ENDOSCOPIC THERAPY FOR ACUTE CHOLECYSTITIS IN OUR HOSPITAL

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**Introduction:** Cholecystectomy is the standard treatment for acute cholecystitis, while in case of increased operative risk, surgery may be postponed or rejected. In such a case, percutaneous or endoscopic gallbladder drainage may be attempted. When percutameous drainage is difficult such as the cases with anticoagulant therapy or anatomical reason, we have performed endoscopic drainage (ETGBS(endoscopic transpapillary gallbladder stent) or ETGBD(endoscopic transpapillary gallbladder drainage) with ETCG(endoscopic transpapillary catheterization into the gallbladder). The aim of the study was to assess the success rate and clinical efficacy,and some technical methods of endoscopic gallbladder drainage in patients with acute cholecystitis.
**Aims & Methods:** A total 36 consecutive patients with acute cholecystitis who received endoscopic drainage between April 2006 and March 2016 were enrolled in the present retrospective study. The technical success rate, clinical success rate, and adverse events rate were evaluated. Technique of ETCG After successful bile duct cannulation, a 0.025 or 0.032-inch guidewire is advanced into the cystic duct and subsequently into gallbladder. (In the lower branch type of cystic duct, seeking of cystic duct is difficult because guidewire is easily bounced to the hepatic side. ENBD tube is useful by fixing pig-tail above the bifurcation) Then catheter is advanced into gallbladder, guidewire is exchanged to the stiff type. Finally, nasobigallbladder drainage tube or stent is placed.
**Results:** The technical success raet was 94%(34/36) and clinical success rate was 100%(34/34). Adverse events rate was 11.1%(4/36:acute pancreatitis(not severe) in 3 cases and injury of cystic duct in 1 case).
**Conclusion:** Ebdoscopic gallbladder drainage with ETCG technique is safe and effective to treat acute cholecystitis with patients who are unsuitable for cholecystectomy or percutaneous drainage. ETCG with ENBD tube is useful especially in the lower branch type of cystic duct.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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TUESDAY, OCTOBER 18, 2016 09:00–17:00
**SURGERY II – POSTER EXHIBITION**

## P0772 DIGESTIVE ALTERATIONS AS EVALUATED BY THE 13C-MTG BREATH TEST IN PATIENTS AFTER BARIATRIC SURGERY

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**Introduction:** The number of patients undergoing bariatric surgical procedures is clearly increasing over the last years due to the increasing prevalence of obesity in the general population. Different bariatric surgical procedures are carried out in obese patients, among them gastric sleeve, gastric bypass and duodenal switch. Gastric and duodenal anatomical changes secondary to these procedures may lead to important disturbances in the digestion and absorption processes. The dynamic of the digestive process may be evaluated by the 13 C-MTG breath test
**Aims & Methods:** Aim of our study was to evaluate the digestive function after different bariatric surgical procedures. Methods: A prospective, cross-sectional study was designed. Patients who underwent any bariatric surgical procedure, gastric sleeve, gastric bypass or duodenal switch, were included. Digestive function was evaluated the 13 C-MTG breath test as previously optimized by our group. The dynamic of the digestive process was defined by the cumulative 13CO2 recovery rate (CRR %), the time to 13 C exhalation peak and the curve of 13CO2 exhalation (% digestion from 0–2, 2–4 and 4–6 hours after meal). Data are shown as median and interquartile range and analysed by the Kruskal Wallis and U-Mann Whitney tests. Sample size was calculated and a total of 90 patients should be included.
**Results:** A total of 94 patients were finally included. 35 patients underwent duodenal switch (49 years, range 29–68, 28 female), 36 gastric bypass (52 years, range 28–68, 28 female) and 23 gastric sleeve (51 years, range 22–70, 19 female). The ability to digest food was quantitatively lower after duodenal switch (CCR $29.02 \pm 21.19\%$) than after gastric bypass (CCR $43.75 \pm 9.02\%$) or gastric sleeve (CCR $49.05 \pm 14.04\%$) ($p < 0.01$). Absorption peak was markedly delayed after duodenal switch (13CO2 exhalation peak at 330 min), compared to gastric bypass (150 min) and gastric sleeve (105 min). In accordance with this, nutrients are digested and absorbed late (4–6 hours after meal ingestion) after duodenal switch, intermediate after gastric bypass (2–4 hours after meal ingestion) and early after gastric sleeve (0–2 hours after meal ingestion) ($p < 0.01$).
**Conclusion:** Significant pathophysiological changes in the processes of digestion and absorption of nutrients are described according to particular bariatric surgical procedures. Duodenal switch alters digestive process more than any other procedure. Compared to gastric bypass, gastric sleeve does not affect digestive function significantly. Whether these differences have an impact on the nutritional status, digestive symptoms, quality of life and long-term morbidity after bariatric surgery deserves further studies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0773 DIFFERENCES IN SURVIVAL AFTER CURATIVE R0-RESECTION FOR KOREAN AND GERMAN GASTRIC CANCER PATIENTS: RESULTS FROM A PROPENSITY SCORE MATCHED ANALYSIS

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**Introduction:** Several retrospective analyses on patients undergoing gastric cancer surgery revealed different survival outcomes between Eastern (Korean, Japanese) and Western (USA, Europe) countries. The reasons remain elusive to date and not only ethnical but also and biological differences were proposed in the past. This propensity score matched analysis investigates surgical and oncologic outcomes between two specialized institutions for gastric cancer in Korea and Germany.

**Aims & Methods:** The local prospectively documented databases were screened for patients undergoing curative (R0,M0) primary surgical resection for gastric cancer between 2002 and 2008. Baseline characteristics were compared using $\chi 2$ testing, and two cohorts were matched using a propensity score matching (PSM). Patients' survival was estimated using Kaplan-Meier methods, and multivariable Cox proportional hazard model was used for comparison of survival outcomes.

**Results:** 3563 from Korea and 275 from Germanywere included in the final analysis. Baseline characteristics demonstrated statistically significant differences for age, tumor-location, pT stage, grading, lymphatic vessel infiltration (LVI), comorbidities, number of dissected lymph-nodes (LN), postoperative complications, lymph-node ratio stage and application of adjuvant chemotherapy. After propensity-score-matching (PSM), 215 patients from the German cohort were matched to Korean patients leading to balanced baseline characteristics for both cohorts. Korean patients demonstrated significantly longer survival than those in Germany both before and after PSM. After stratification for each UICC-stage the same trend was detected in any of the the UICC-stages. However, significant survival differences could be detected only for UICC III after PSM.

**Conclusion:** Differences in overall survival between Korean and German gastric cancer patients persist after balancing for possible confounders by propensity score matching.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0774 PERIOPERATIVE TRANSFUSION OF BLOOD PRODUCTS IN GASTRIC CANCER PATIENTS NEGATIVELY INFLUENCES ONCOLOGIC OUTCOME – A RETROSPECTIVE PROPENSITY SCORE WEIGHTED ANALYSIS

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**Introduction:** The influence of perioperative transfusion (PT) on outcome following surgery for gastric cancer remains controversial, with randomized trials lacking and observational series confounded by patient risk factors.

**Aims & Methods:** Data from 610 patients who underwent curative surgery for gastric cancer(R0/M0) in a German Univeristy hospital from 2001 to 2013 were included. Kaplan-Meier survival curves and Cox proportional hazards regression were applied to determine the association of PT and clinical and patient risk factors for overall and relapse-free survival. Propensity score analysis was performed to adjust for observational biases in reception of PT.

**Results:** Higher UICC/AJCC-stages ($p < 0.001$), postoperative complications and severity according to the Clavien-Dindo-classification ($p < 0.001$), perioperative blood transfusion (PT) ($p = 0.02$), higher age ($p < 0.001$) and neoadjuvant chemotherapy ($p < 0.001$) were related to increased mortality rates. Higher UICC-stages ($p < 0.001$), neoadjuvant chemotherapy ($p < 0.001$) and type of surgery ($p = 0.02$) were independently associated with increased relapse-rates. Patients were more likely to receive PT with higher age ($p = 0.05$), surgical extension to adjacent organs/structures ($p = 0.002$), tumor-location ($p = 0.003$) and female gender ($p = 0.03$). In the adjusted propensity score weighted analysis, PT remained associated with an increased risk of death (HR: 1.30, 95%CI: 1.01–1.68, $p = 0.04$).

**Conclusion:** Due to a potential independent association of perioperative blood transfusions with negative influence on patient survival following oncologic resection, application of blood products should be considered carefully in gastric cancer patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0775 ESOPHAGECTOMY FOR ESOPHAGEAL CANCER WITH SUPRACLAVICULAR LYMPH NODES METASTASIS

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**Introduction:** The supraclavicular lymph nodes metastasis has been recognized as distant lymph nodes metastases (M1 LYM) according to UICC 7th.

**Aims & Methods:** The aim of this study is to investigate the usefulness of esophagectomy in patients with supraclavicular lymph nodes metastasis. Two hundred eighty-two patients, who underwent R0 esophagectomy for thoracic esophageal squamous cell carcinoma between 1996 and 2012, were analyzed by univariate and multivariate analysis. The median follow-up duration was 62 (range from 3 to 239) months.

**Results:** There were 252 males and 30 females, with a median age of 63 years (range 39–87 years). Of the 282 patients, 90 (32%) had pT1 cancer, 46 (16%) had pT2 cancer, 134 (48%) had pT3 cancer, and 12 (4%) had pT4 cancer. The number of patients at N status N0/N1/N2/N3 were 107 (38%)/ 87 (31%)/ 61 (22%)/ 27 (9%). Twenty-three patients (7%) had supraclavicular lymph nodes metastasis (M1 LYM). Three-field lymphadenectomy was performed in 173 (61%) patients and Two-field lymphadenectomy was performed in 109 (39%) patients. The median number of resected lymph nodes was 60 (range, 16–151). The overall 5- and 10-year survival rates in all patients were 59% and 44%, respectively. By univariate analysis, gender (male; $p = 0.0032$), post operative complication (absent; $p = 0.0433$),the depth of tumor invasion (pT1,T2; $p < 0.0001$), lymph nodes metastasis (absent; $p < 0.0001$), histopathological grading (G1; $p < 0.0001$), lymphovascular invasion (absent; $p < 0.0001$), tumor length (6 cm $\geq$; $p = 0.0407$), and the number of resected lymph nodes ($\geq$60; $p = 0.0092$) were associated with improved survival. The 5-year survival rate of patients with supraclavicular lymph nodes metastasis was 43%, compared to 61% those without supraclavicular lymph nodes metastasis ($p = 0.0707$). Supraclavicular lymph nodes metastasis did not significantly affect survival. In multivariate analysis, gender (female vs. male: hazard ratio 0.435; 95% confidence interval 0.195–0.835; $p = 0.0102$), post operative complication (absent vs. present: hazard ratio 0.615; 95% confidence interval 0.434–0.863; $p = 0.0047$), the depth of tumor invasion (pT1,T2 vs. pT3,T4: hazard ratio 0.420; 95% confidence interval 0.280–0.622; $p < 0.0001$), lymph nodes metastasis (absent vs. present: hazard ratio 0.596; 95% confidence interval 0.401–0.870; $p = 0.0069$), histopathological grading (G1 vs G2,G3: hazard ratio 0.494; 95% confidence interval 0.341–0.702; $p < 0.0001$), the number of resected lymph nodes ($\geq$60 vs 60$>$: hazard ratio 0.558; 95% confidence interval 0.398–0.777; $p = 0.0005$) were found to be independent prognostic factors. In patients with supraclavicular lymph nodes metastasis, tumor length (8 cm vs. $\geq$8 cm; hazard ratio 0.300; 95% confidence interval 0.092–0.851; $p = 0.0232$), the number of lymph nodes metastasis (3$\geq$ vs. $\geq$4: hazard ratio 0.357; 95% confidence interval 0.112–0.984; $p = 0.0464$) were found to be prognostic factors.

**Conclusion:** Our findings suggest that esophagectomy may be effective some patients with the supraclavicular lymph nodes metastasis, in particular the number of lymph nodes metastasis is 3 or less, or the tumor length is less than 8 cm.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0776 FEASIBILITY AND EFFICACY OF MODIFIED PERORAL ENDOSCOPIC MYOTOMY (LIU-POEM) IN PATIENTS WITH ACHALASIA: A RETROSPECTIVE COMPARISON STUDY

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**Introduction:** Esophageal achalasia is a primary motility disorder involving absence of esophageal peristalsis, failure of the lower esophageal sphincter (LES) to relax, and cardiac diastolic dysfunction. Peroral endoscopic myotomy (POEM) has emerged as one approach to treating esophageal achalasia. Although POEM is credited with high success rates in the treatment of achalasia, the submucosal tunneling is time consuming and commonly requires one-third to two-third of the total operation time. For improvement of POEM procedure, we modified the POEM procedure by limiting myotomy and tunnellization into one step. We named this modified peroral endoscopic myotomy Liu-POEM.

**Aim** To compare Liu-POEM and conventional POEM for the treatment of achalasia, analyze the clinical outcomes of each method, and evaluate the feasibility and efficacy of Liu-POEM.

**Methods** 30 patients with achalasia were included in the Liu-POEM group, and 30 patients were included in the conventional POEM group retrospectively. The clinical characteristics, therapeutic success, procedure-related parameters and adverse events were compared.

**Results:** Liu-POEM was successful in all. Meanoperation time of conventional POEM was 51.2 min (range 24–119 min) and Liu-POEM was 27.2 min (range 15–62 min). The different operation times were statistically significant ($p < 0.001$). Length of myotomy in POEM group was 9.9 cm and the other group was 8.6 cm ($p = 0.054$). The mean number of mucosotomy-closure clips are 12 and 10 using in POEM and Liu POEM procedure respectively ($p = 0.006$). The symptom remission rates were 100% in boths groups. Their Eckardt scores were less than 3. Only 3 patients in POEM groups sufferred mild subcutaneous emphysema, but they recover without any special treatment in one day.

**Conclusion:** Liu POEM and POEM for the treatment of achalasia has the same therapeutic effect. Liu POEM leads to a significant decrease in POEM procedure time and possibly contributing to a lower rate of complications. Further studies have to confirm this.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0777 PREVENTION OF FISTULA AFTER DISTAL PANCREATIC RESECTION


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**Introduction:** The most common and the most severe complication to a distal pancreatic resection is the forming of a postoperative pancreatic fistula (POPF). A frequency of 30–60% has been reported. To reduce the frequency of POPF the use of somatostatin, dividing pancreas with a stapler, suturing and/or covering the remaining part of the cut pancreas with glue have all been assessed in trials without any of the methods showing superiority. In previous studies, the combination of stapling technique and resorbable staple line reinforcement has shown both positive and negative influence on POPF frequency. The present study is a prospective, randomized, controlled multicentre trial (RCT) comparing reinforcement with resorbable mesh (The Biodesign™ Surgisis® staple reinforcement, COOK® Medical) or not at the site of stapling division of the pancreas in distal pancreatic resection.

**Aims & Methods:** Patients planned for open or laparoscopic distal pancreatic resection with or without splenectomy, at four Swedish tertiary referral centres, were informed about the study. On accepting to participate they were randomized peroperatively, after confirming that resection could take place, to either reinforcement or not at the division site. Primary outcome was a pancreatic fistula or leakage, in accordance with the definition of a pancreatic fistula made by ISGPF's (International study group of pancreatic fistula), and the number of days to healing/drain evacuation.

**Results:** 105 patients (51 female/54 male) aged 62.9 (28–89), ASA 2 (median) were randomized to either reinforcement (54) or no reinforcement (51) on the stapler instrument dividing the pancreas. In the group with reinforcement 22.2% of the patients developed a fistula (12/54) and in the group without reinforcement 39.2% (20/51) developed a fistula ($p = 0.043$). Once a fistula had occurred there was no difference in healing time/ days to drain removal between the groups.

**Conclusion:** Reinforcing the stapler line with a resorbable mesh when performing a distal pancreatic resection results in a reduced risk of developing a POPF.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0778 RISK-BASED PATIENT SELECTION IN OPEN AND MINIMALLY-INVASIVE DISTAL PANCREATECTOMY: AN ACS-NSQIP STUDY


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**Introduction:** Patient selection criteria which optimize outcomes after minimally invasive distal pancreatectomy [MIDP] remain unknown. As a result, widespread adoption of this surgical technique has been delayed with resulting misallocation of its potential benefits. Our two aims were to assess current case selection factors for MIDP and to identify actual risk factors for adverse outcomes compared to open distal pancreatectomy [ODP].

**Aims & Methods:** Retrospective cohort study of elective ODP versus MIDP, using the pancreas-targeted database of the American College of Surgeons National Surgical Quality Improvement Program® (ACS-NSQIP®), collected at 106 participating centers in 2014. Excluded were patients requiring neoadjuvant treatment or having pancreatitis as only diagnosis. The primary outcome was a composite major morbidity metric, reflecting major surgical and medical complications, including extended length of stay, reoperation, and death. Two multivariable models were used to detect currently applied selection factors and to determine actual independent risk factors of composite major morbidity, adjusting for baseline differences and incorporating approach interactions.

**Results:**

**Table:** Perioperative and postoperative outcomes, unmatched cohorts.

| | ODP (472) | MIDP (456) | P-Value |
|---|---|---|---|
| Operative time, median (i.q.r.), min. | 199 (156–266) | 215.5 (162–275) | .166 |
| Multivisceral procedure, No. (%) | 95 (20.1%) | 40 (8.8%) | <.001 |
| Blood transfusion for bleeding (<72 hrs), No. (%) | 65 (13.8%) | 23 (5.0%) | <.001 |
| Mortality within 30-days, No. (%) | 5 (1.1%) | 3 (0.7%) | .508 |
| Unplanned reoperation, No. (%) | 13 (2.8%) | 7 (1.5%) | .201 |
| Length of say, median (i.q.r.), days | 6 (5–7) | 5 (4–6) | <.001 |
| Unplanned readmission, No. (%) | 85 (18.0%) | 52 (11.5%) | .005 |
| Composite major morbidity*, No. (%) | 111 (23.5%) | 61 (13.4%) | <.001 |

In total, 928 patients underwent ODP (472) or MIDP (456) using a laparoscopic or robotic approach. Current selection factors for MIDP were presence of benign disease (odds ratio [OR] 1.56, 95 per cent confidence interval [CI] 1.10–2.21) and body-mass-index between 30–40 (OR 1.41, CI 1.04–1.91). Current selection factors against MIDP were pancreatic ductal adenocarcinoma presence (OR 0.45, CI 0.31–0.64), benign tumor size over 5 centimeters (OR 0.40, CI 0.23–0.67), and multivisceral resection (OR 0.39, CI 0.26–0.59). In patients lacking potential risk factors, MIDP was associated with a significantly lower risk of composite major morbidity compared to ODP (OR 0.37, CI 0.14–0.97). Diabetes was the only risk factor which added significantly to the baseline odds of composite morbidity in MIDP compared to ODP (OR 2.55, CI 1.14–5.71; $P = 0.023$).

**Conclusion:** Current patient selection factors for MIDP in the United States do not mitigate the actual odds of postoperative composite major morbidity. Diabetes was the only patient risk factor associated with significant additive risk of composite major morbidity after MIDP compared to ODP. No other risk factors were identified that justify restricting the utilization of a minimally invasive technique to perform distal pancreatectomy. The mechanism behind the impact of diabetes on outcomes after MIDP requires further study.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0779 ROLE OF EXTERNAL JEJUNAL DRAINAGE AND PERIOPERATIVE SERUM ALBUMIN EVALUATION IN PREDICTION AND MANAGEMENT OF PANCREATIC FISTULA


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**Introduction:** Despite improvements in surgical techniques, instruments and perioperative management, postoperative pancreatic fistula (POPF) remains a serious complication after pancreaticoduodenectomy (PD). The aim of the

present study was to evaluate the potential role of perioperative clinical variables of patients in predicting pancreatic fistula and the impact of external jejunal drainage in management of complications.
**Aims & Methods:** 52 patients underwent PD for pancreas cancer between 2010 and 2015 at our institution. In all cases a Whipple procedure was performed with external drainage tube in the jejunal segment anastomosed to pancreatic stump and hepatic duct. Pancreatic fistula have been assessed according to ISGPF criteria: grade B and C were defined as "POPF". Surgical complications have been graded according to Clavien scale: grade III-IV-V were considered serious complications. Perioperative clinical variables were evaluated and investigated with univariate and multivariate analyses.
**Results:** 12 patients (23.1%) developed Grade B POPF. No Grade C fistulas were detected. Perioperative (within 30days) deceases were 2 (3.8%), both for heart failure. Second surgery was performed on 3 patients (5.7%): 1 for gastrojejunal leak (1.9%), 1 for splenic artery bleeding (1.9%) and 1 for bilioenteric leak (1.9%). 1 patient (1.9%) developed a splenic artery pseudoaneurysm treated with angiographic embolization, 1 patient (1.9%) developd a self-limited gastrointestinal bleeding. At univariate analysis POPF correlated with soft pancreas ($p = 0.02$), low levels of postoperative day (POD) 1 albumin (mean value $20.66 \pm 2.99$ g/L vs $24.79 \pm 4.10$ g/L in patients without POPF; $p = 0.005$) and POD 1 albumin decrease ($16.33 \pm 5.34$ g/L vs $11.31 \pm 5.05$ g/L in patients without POPF; $p = 0.019$). No significant correlations with POPF were demonstrated for age, surgical time and preoperative albumin levels. These data have been confirmed at multivariate analysis (Tab.1). Other serious complications (grade III-V) were correlated with low level of POD 1 albumin (mean $21.70 \pm 3.14$ g/L vs $24.40 \pm 4.08$ in patients without serious complications; $p = 0.015$) and high POD1 albumin decrease (mean $14.45 \pm 5.42$ g/L vs $11.15 \pm 5.39$ in patients without serious complications; $p = 0.037$).

**Table 1:** Multivariate analyses of clinical variables in relation to postoperative pancreatic fistula grade B or C after pancreaticoduodenectomy.

| Parameters | OR | p-Value |
|---|---|---|
| Age | 2.513 | .091 |
| Preoperative Albumine | 1.198 | .311 |
| POD1 Albumin (g/L) | 5.872 | .005 |
| POD1 Albumin Decrease (g/L) | 4.317 | .019 |
| Surgival Time | 1.096 | .342 |
| Pancreas Consistency | 5.402 | .008 |

POD: post-operative day

**Conclusion:** Postoperative pancreatic fistula significantly correlates with postoperative level and decrease of albumin, demonstrating a latent impairment in metabolic and nutritional status of some patients more prone to develop POPF and other major complications. These data suggest a predictive role of nutritional status assessment that could be useful in postoperative management of patients. Furthermore, external jejunal drainage of bilious, pancreatic and intestinal fluid seems to be helpful in prevention of grade C fistulas, reducing morbidity and promoting a conservative management of patients with POPF.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0780 TOTAL PANCREATECTOMY: SHORT-TERM AND LONG-TERM OUTCOMES OF THE APANCREATIC STATE

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**Introduction:** Complete pancreatic resection, or Total Pancreatectomy (TP), represents an increasing indication for diffuse pancreatic disease. While several studies have demonstrated that improvements in the perioperative care have decreased short-term morbidity and mortality, only small series have investigated long-term impact of the apancreatic state. With this study we aim to evaluate short-term and long term outcomes following total pancreatectomy. In particular quality of life (QoL) of long term survival patients has been investigated using validated questionnaires with respect to the indication for surgery.
**Aims & Methods:** Patients who underwent TP between 2000 and 2015 at the Department of General and Pancreatic Surgery, Verona University (VU) and at the Department of Hepatobiliary and Pancreatic Surgery, Johns Hopkins University (JHU), were retrospectively identified from prospectively collected databases. Possible risk factors associated with the development of perioperative complications were evaluated using univariate and multivariate regression models. Long-term outcomes were assessed using an original specific survey, and validated QoL questionnaires: Short Formula36 (SF-36), EORTC-PAN26, Audit of Diabetes-Dependent (ADD) QoL. In particular correlation analyses and linear logistic regressions investigated the association between physical (PCS) and mental composites (MCS) at the SF-36 and results at the DD-AWI and at the PAN-26.
**Results:** 329 patients underwent TP at VU and JHU between 2000 and 2015. Postoperative morbidity was 59.3%, 64 (22.4%) patients experienced major surgical complications (Clavien-Dindo grade III-IV) and 17 (5.1%) patients died within 90 days from TP. At multivariate analysis age ($P = 0.014$, OR 1.041, 95% CI 1.008–1.074) and duration of surgery were independent predictors for major complications ($P = 0.008$, OR 1.005, 95% CI 1.001–1.008). 152 patients with more than 12 months of follow up after surgical resection were enrolled in the cross-sectional study. Among them, 94 replied to the questionnaires. The median follow-up from surgery was 63 months (20–109). SF36 reported no difference in the general health perception ($P = 0.069$) and in the body pain ($P = 0.717$) before and after surgery, while PCS and MCS were both significantly reduced (respectively: $P = 0.047$ and $P = 0.019$). At the EORTC-PAN, the most affected symptoms were digestive symptoms (mean 47.6% SD 31.1) and altered bowel habit (mean 42.8% SD 32.2). The ADD-QoL shows that diabetes has a negative impact in the daily life, with an overall average weighted impact score (AWI) of −1.9 (±2.1). Reduced MCS and PCS were correlated with male gender and a higher score at the PAN 26. Linear regression model shows that persistent abdominal pain after TP was negatively associated with the SF-36 PCS and MCS (PCS: ß −0.38, 95% CI −0.80 to −0.1, $P = 0.004$; MCS: ß −0.351, 95% CI −0.7 to −0.11, $P = 0.007$).
**Conclusion:** Short-term outcomes for TP are aceptable. Age and a long time operation are risk factors associated with major complications after surgery. Patient's General Health perception appears not to be affected from surgery, but when specifically investigated both PCS and MCS are downgraded. Diabetes, digestive symptoms and altered bowel habit mainly affect the QoL after surgey, however they do not significantly correlates with PCS and MCS. The persistence of abdominal pain and its intensity after surgery directly correlate with both physical and mental limitations. Control of abdominal pain may significantly improve QoL outcomes after surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0781 SOLID PSEUDOPAPILLARY TUMOURS OF THE PANCREAS: SPECIFIC PATHOLOGICAL FEATURES PREDICT THE LIKELIHOOD OF POSTOPERATIVE RECURRENCE

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**Introduction:** Since their introduction in the WHO classification, the incidence of solid pseudopapillary tumours (SPTs) of the pancreas has progressively increased mainly because of the widespread use of cross-sectional imaging. Few recent studies have analysed the biological behaviour of SPTs, but reliable data on long-term follow-up are needed.
**Aims & Methods:** Retrospective analysis of two Institutions with high case-load, The Department of General Surgery – Pancreas Institute, University of Verona Hospital Trust and the Department of General Surgery, Massachusetts General Hospital, Harvard Medical School was carried out. Data from 131 consecutive resections for SPT performed during the last 3 decades were collected and analysed.
**Results: Results** The majority of patients were female (86.3%) with a median age of 33 (7 – 68) years. The prevalent location was the pancreatic tail (33.5%). Applying the WHO criteria, 16 (12.2%) SPTs were considered malignant due to the presence of at least pancreatic parenchyma invasion (9.9%), perineural invasion (4.6%), and/or angiovascular invasion (2.3%). After a median of 62 months after surgery, only two patients had a recurrence (1.5%). Both of them fulfilled the WHO criteria for malignant SPT (vs. 10.7% of those who did not recur, $p = 0.01$), had an infiltrative growth pattern (vs. 10.8%, $p = 0.01$), pancreatic parenchyma invasion (vs. 9.7%, $p = 0.01$) and capsular invasion (vs. 4.9%, $p = 0.004$).
**Conclusion:** Overall, SPTs are associated with excellent survival results after surgical resection. Disease recurrence is extremely rare, and might occur if the primary tumour presents with either pancreatic parenchyma or capsule invasion.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0782 ACUTE CHOLECYSTITIS CLASSIFICATION. ANALYSIS AND EVALUATION OF THE NEW DIAGNOSTIC CRITERIA AND SEVERITY OF ACUTE CHOLECYSTITIS REVISED BY TOKYO GROUP 2013

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**Introduction:** Acute cholecystitis is one of the most common causes of surgery in the emergency room services around the world. Since 2007, and later in 2013, it has been used them for this common disease proposed by the Consensus of Tokyo (TG07 and TG13). Gastroenterologist and Surgeons around the World have used as the gold standard to diagnose and determining the severity of the AC and then decide the timely treatment. Unfortunately, we have found there are many differences between Tokyo (TG13) Severity Assessment Criteria and transoperative features in Laparoscopic Cholecystectomy. TG13 grade Acute Cholecystitis in three groups: Grade III (severe) acute cholecystitis is associated with dysfunction of some organs or systems; Grade II (moderate) Acute Cholecystitis is associated with any one of the following conditions (Leukocytosis $>18{,}000/mm^3$, Palpable tender mass in the upper abdominal quadrant, duration of complains $>72$ h or Marked local inflammation) and Grade I: acute cholecystitis does not meet the criteria of ''Grade III'' or ''Grade II''. We have propose a table which collects the macroscopic transoperative features in laparoscopic cholecystectomy in cases of acute cholecystitis and allows to grade the severity of the cholecystitis, and evaluate the the concordance with the ''New diagnostic criteria and severity assessment in Tokyo guidelines'' and histopathological features. The conclusion was that concordance grade DTFT and Tokyo criteria was little almost nill. These findings suggest a reconsideration to stake new classification criteria to grading acute cholecystitis.
**Objective:** To review the database of our study and try to find any explanation about the non concordance between Tokyo criteria, the histopatologycal features and our proposed table of macroscopic transoperative features in laparoscopic cholecystectomy, in cases of acute cholecystitis.
**Methodology:** 91 medical records of patients who were attended with the diagnosis of ''Acute Cholecystitis'' (AC) were reviewed (clinical files, laboratories results and imaging studies, dvds cholecystectomy video). This is a cohort study, it was double blind. At the end we summed all the items and we classified the results in phases ranging from a 1 to a 3 phase according to its score (mild, moderate, and severe severity). A kappa test was realized to assess the degree of agreement between our DTFT and the Tokyo criteria using the software STATA v.13.
**Results:** The medical records of 91 patients treated for acute cholecystitis were reviewed, they were classified according to the criteria for severity of Tokyo in Phase I (mild) 22 pac (24.17%), stage II (moderate) 63 pac (69.23%) are reviewed and Phase III (severe) 6 patients (6.59%). Of these the criteria for classification in grade III was 3 pac (50%) creatinine $>2$ mg/dl; 2 pac (33.33%) neurological deficit; and one pac (16.66%) with platelet $<100{,}000/mm^3$ account. Of the 63 patients classified as Stage II (moderate) variable selection was: 58 pac (92.06%) the evolution of the disease $>72$ hrs, 6 pac (5.52%) leukocytes $>18{,}000/mm^3$. It is noteworthy that the duration of the classification variable condition, obviously would deduce that this affects other systems or organs, however, to review the rest of the parameters are not altered by this variable.
**Conclusion**: Therefore, it may be desirable to rethink the criteria of severity, and this allows to have more consistent with the other scales, which in turn also require review and redefine its variables. It is fair to say that this puts us all on the way to improve and unify criteria and classifications
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0783 MODIFIED FOLFOX6 AND BEVACIZUMAB AS NEOADJUVANT CHEMOTHERAPY FOR PATIENTS WITH POTENTIALLY CURABLE BILOBAR LIVER METASTASES FROM COLORECTAL CANCER

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**Introduction:** Even though patients with colorectal cancer (CRC) and liver metastases have a poor prognosis, they can benefit from perioperative chemotherapy and complete extirpation of the diseases. Oxaliplatin-based chemotherapy with bevacizumab has been widely reported to improve outcomes with metastatic CRC.
**Aims & Methods:** The objective of the present study is to elucidate impact of neoadjuvant chemotherapy based on oxaliplatin and bevacizumab on surgical complications and survival benefit after hepatectomy in patients with potentially curable synchronous bilobar liver metastases. Twenty-three patients with potentially curable bilobar liver metastases from CRC were eligible for this prospective single-center, nonrandomized trial during a period between September 2008 and December 2014 (NAC group). The study group consisted of 15 men and 8 women, with median age of 62.1 (range 52 to 79) years. Eligible criteria included synchronous liver metastases and metastatic liver disease developed within one year after resection of the primary lesions. Patients received biweekly oxaliplatin of $85\,mg/m^2$, folic acid of $200\,mg/m^2$, a bolus 5-fluorouracil of $400\,mg/m^2$, and continuous 5-fluorouracil of $2400\,mg/m^2$ for 46 hours (modified FOLFOX6) plus bevacizumab of 5 mg/kg for 6 cycles. The sixth cycle of neoadjuvant chemotherapy (NAC) did not include bevacizumab, resulting in 4 weeks window-time between the last administration of bevacizumab and hepatectomy. No additional postoperative adjuvant chemotherapy was performed. Overall survival (OS) and progression free survival (PFS) rates were compared with 13 patients who underwent hepateictomies for synchronous multiple bilober liver metastasis from CRC without NAC during 2002 and 2008 (non NAC group).
**Results:** Synchronous liver diseases were observed in 20 (87.0%). In the remaining 3 patients, liver metastases developed within one year after primary surgery for CRC. Objective response to NAC was achieved in 6 patients (26.1%), and 21 patients (91.3%) underwent liver resection. Two patients were excluded from hepatectomies because of progressive diseases. The liver surgery included 5 hemihepatecitomies, 10 sectorectomies, and 6 partial resections of the liver with median operative time of 207 minutes and median blood loss of 340 mL without blood transfusion. Median size of the liver tumor was 3.7 cm in diameter and number of the tumors was 3.6. Any posthepatectomy morbidity or morbidity was observed in NAC group. Three- and five-year PFS of the NAC group were significantly better than those of non-NAC group (34.4% and 34.4% respectively (median survival time, 12.8 months) vs. 18.2% and 18.2% (9.0 months), $P=0.038$). And three- and five year OS of NAC group were slightly better without significant difference (72.3% and 21.1% (48.9 months) vs. 41.5% and 16.8% (31.2 months), $P=0.063$). Among the hepatectomized patients of NAC group, 13 patients (61.9%) developed recurrence, and initial recurrent deposits were observed in remaining liver in 6 patients (46.2%), lymph nodes in 6, lung in 4 and peritoneum in 2 (redundant included).
**Conclusion:** Our data suggest that NAC of 6 cycles with modified FOLFOX6 and bevacizumab can be safely administered until 4 weeks before liver resection without increasing perioperative complications and may provide better OS and PFS with good local control of the liver in patients with synchronous bilobar multiple liver metastases from CRC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0784 PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE – FIRST STEP IN THE PALLIATIVE TREATMENT OF MALIGNANT BILIARY OBSTRUCTION?

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**Introduction:** Obstructive jaundice is a frequent complication, occurring in patients with biliary tract and periampullary malignancies. It's a symptom of advanced stage of the disease and poor prognosis. Biliary decompression is necessary in order to prevent patients from more serious complications and allow them to receive further treatment.
**Aims & Methods:** The aim of this study was to evaluate the clinical outcomes and possible benefit of an ultrasound-guided percutaneous transhepatic biliary drainage as the first step in the palliative treatment of malignant biliary obstruction. Retrospective review of patients undergoing percutaneous transhepatic biliary drainage from 2014 to 2015 at the Department of Surgery, Hospital of the Lithuanian University of Health Sciences was performed. Patients were reviewed for demographic features, laboratory tests, complications, outcomes (reduction in serum bilirubin level), hospital stay and mortality rate.
**Results:** During the study period 99 patients (43.4% males ($n=40$)) with median age of $68.67 \pm 11.02$ (range 44–95) received 124 successful biliary drainage procedures for malignant obstructive jaundice. Prior the percutaneous drainage procedure 58 patients (58.6%) were unsuccessfully treated by endoscopic retrograde cholangiopancreatography (ERCP). Forty patients (40.4%) were diagnosed with periampullary tumours, thirty patients (30.3%) had proximal/hilar cholangiocarcinoma and 29 (29.3%) patients had biliary obstruction due to liver metastasis. Acute cholangitis before drainage procedure was present in 52 (52.5%) patients. After drainage procedure total serum bilirubin value decreased in 87 (87.9%) patients (from $293.72 \pm 131.9\,\mu mol$ to

193.11 ± 117.49 μmol, $p < 0.05$). Reduction in the levels of Gamma-glutamyl transferase and Alkaline phosphatase was observed in 94 (94.9%) patients. Seventy patients (70.7%) underwent additional interval procedures. In 62 (88.6%) cases percutaneous transhepatic biliary stenting was performed. The mean hospital stay was 25.49 ± 17.97 days (after percutaneous drainage −19.95 ± 17.28 days). Thirty-four (34.3%) patients developed drainage related complications, with drainage catheter dislocation being most common (70.6% (n = 24)). Hospital mortality rate reached 27.3% (n = 27) with no drainage-related deaths.
**Conclusion:** Percutaneous transhepatic biliary drainage is safe and effective method to reduce malignant obstructive jaundice, when other drainage methods are unavailable. Percutaneous transhepatic biliary drainage acts as a first step in further palliative treatment of these diseases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0785 RBC DISTRIBUTION WIDTH (RBC-DW) AND ACUTE CHOLECYSTITIS. CORRELATION BETWEEN THE RBC DISTRIBUTION WIDTH (RBC-DW) AND THE DESCRIPTIVE TRANSOPERATIVE FEATURES TABLE (HGM), THE NEW DIAGNOSTIC CRITERIA AND SEVERITY ASSESSMENT IN TOKYO GUIDELINES

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**Background:** Acute cholecystitis is one of the most common causes of surgery in the emergency room services around the world. Since 2007 and later 2013, the diagnostic criteria and severity assessment criteria have been used for this widespread disease. Nevertheless, a description of transoperative features hasn't been standardized, so it has been impossible to classify or grade acute cholecystitis. Nowadays, with the aid of our proposed "Descriptive transoperative features table" (DTFT), we are now able to grade the severity of acute cholecystitis. The rheologic changes of red blood cells (RBC) and their physiopathological role during inflammation are not completely understood. Previous studies have founded important alterations in RBC shape and functional disturbances during sepsis and inflammation. We have noticed that there are many differences between the Tokyo Classification (2013), the transoperative features and Histopathology features. Our objective was to study the variations of RBC distribution width (RBC-DW) in patients with acute cholecystitis and its relation with the severity of each case.
Aims & Methods:
**Objective**: To study the variations of RBC distribution width in patients with acute cholecystitis and its relation with the severity of each case and to find the concordance with the "New diagnostic criteria and severity assessment in the Tokyo guidelines", the table in which the macroscopic transoperative features of laparoscopic cholecystectomy and histopathological features.
**Methodology**: Sixty-two medical records of patients who were attended with the diagnosis of "Acute Cholecystitis" (AC) were reviewed (clinical files, laboratories results and imaging studies, and cholecystectomy videos). This is a cohort study, it was double blind. In the stage, we added all the scores and classified the results in phases ranging from phase I to a phase III according to their score (mild, moderate, and severe severity). A kappa test was done to assess the degree of agreement between The RBC Distribution Width (RBC-DW) and our DTFT, the Tokyo criteria and histopatological features using the software STATA v.13.
**Results:** There were 62 patients: 39 women (in the range of 21 to 79 years old) with a mean age of 56.75 years, and 23 men (range of 28 to 76) with a mean of 55.38 years. They were grouped according to the Tokyo criteria in: mild, 13 (20.96%); moderate, 43 (69.35%); and severe 6 (9.67%); DTFT criteria I: 13 (20.96%), II: 29 (46.77%), III: (29.03%) and IV: 1 patient; and by histopatological features: Acute Cholecytitis (AC) non gangrenous: 23 (37.09%), CA with microscopic foci of necrosis: 35 (56.45%) and acute gangrenous cholecystitis 4 (6.15%). The RBC-DW was in normal range in the most of cases, except in fase III of Tokyo criteria where it was elevated in 66.6% of the cases. According to the kappa index, the degree of agreement between RBC-DW, Tokyo criteria,DTFT criteria and histopathological features criteria was fair.
**Conclusion**: We also concluded that we need to study a bigger population to acutely describe an association between this variables and RBC-DW. The relationship between RBC-DW and severity assessments scores has to be defined with future studies. And we suggest a reconsideration be taken if we want to advance a new set of classification criteria for grading acute cholecystitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0786 CONTEMPORARY APPROACHES TO CHOOSING SURGICAL TREATMENT FOR PATIENTS WITH COMPLICATED FORMS OF CHRONIC PANCREATITIS

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**Introduction:** Cronic pancreatitis (CP) is a progressing inflammatory process in the pancreas that results in complete destruction of gland tissue, derangement of digestion, development of diabetes mellitus, and manifest pain syndrome. Over the last thirty years, we have witnessed a more than double increase in the number of CP patients.
**Aims & Methods:** We analyzed the results of surgical treatment of 144 patients with complicated forms of CP who underwent surgical treatment at the department of surgery of the Ivano-Frankivsk Regional Clinical Hospital, Ukraine, among them 133 (92.3%) men and 11 (7.7%) women aged 21 to 72. To diagnose CP and its complications we used: laboratory tests, ultrasonography, endoscopic retrograde cholangiopancreatography, computer tomography, magnetic resonance cholangiopancreatography, intraoperative measurement of bile pressure. The quality of patients' life in the remote postoperative periods was considered the criterion of surgical treatment efficiency. Assessment of the remote results of surgical treatment was done by examining the patients, ultrasonography, and filling out the «Short Form Medical Outcomes Study» (SF-36) questionnaire, which allows assessing physical and psychoemotional conditions of the surveyed separately.
**Results:** Surgical treatment was applied to 144 patients with CP. In 54 (37.5%) patients, CP was complicated by dysfunction of adjacent organs. Particularly, these were biliary hypertension (BH) in 36 (25%) patients and chronic duodenal obstruction (CDO) in 8 (5.5%) patients. In 5 (3.5%) patients, BH was combined with CDO, and another 5 (3.5%) patients had a combination of BH, CDO and venous hypertension (VH) of the portomesenteric area. Indications for surgical treatment were as follows: persistent pain syndrome and inefficiency of pharmaceutical treatment; manifest duct hypertension due to fibrotic CP with dilatation of pancreatic ducts and pancreatic juice hypertension in hem or calculous CP with manifest intrapancreatic hypertension – 48 (33.3%) patients; fibrocystic CP with formation of retention cysts, pseudocysts and external fistula of the pancreas – 27 (18.7%) patients; fibrous-degenerative CP with involvement of adjacent organs and their dysfunction (BH, CDO, VH, and their combination) −54 (37.5%) patients; pancreatic pseudotumor and assumption of a pancreas tumor – 10 (6.9%) patients. Resection surgeries were performed in (43.4%) patient (pancreaticoduodenal resection (PDR) – 5 (3.5%), Frey's procedure – 44 (30.5%), Berne modification – 2 (1.4%), distal pancreas resection – 10 (7%). Draining operations were performed in 74 (51.4%) patients, palliative surgeries – in 9 (6.2%) patients. In 16 patients with CP accompanied by signs of BH, intraoperative monitoring of biliary pressure was performed, which allowed determining the appropriateness of the surgery for the elimination of BH.
**Conclusion:** The results of surgical treatment were traced in 43 (29.8%) patients in the period from 6 to 36 months and appeared to be good and satisfactory. Life quality indicators were better in patients who underwent resection surgeries on the pancreas.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0787 IMPACT OF PRE-TRANSPLANT SARCOPENIA AND SEQUENTIAL CHANGES IN SARCOPENIC PARAMETERS AFTER LIVING DONOR LIVER TRANSPLANTATION

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**Introduction:** Sarcopenia is characterized by muscle mass depletion and decrease in muscle power or physical activity. We reported that preoperative low skeletal muscle mass was an independent risk factor for survival after living donor liver transplantation (LDLT) in a retrospective study (1).
**Aims & Methods:** The present study prospectively investigated the impact of pretransplant sarcopenia on survival after LDLT. Moreover, we examined sequential changes in sarcopenic parameters after LDLT. Seventy-two consecutive adult patients who underwent LDLT at our institute between January 2013 and October 2015 were enrolled in this study. Median patient age was 55 (range, 21–68), 38 (53%) were male, median MELD score was 18 (range, 6–41). Sarcopenia was assessed by the measurement of skeletal muscle mass (SMM) obtained by a multifrequency body composition analyzer (InBody 720®) and handgrip strength (HS). We defined patients with sarcopenia as those with low SMM (< 90% of the standard SMM) and low HS (< 26 kg for men, < 18 kg for women). The impact of pretransplant sarcopenia on short-term survival and sequential changes in sarcopenic parameters including SMM and HS were analyzed.
**Results:** The overall survival rate in patients with preoperative sarcopenia (n = 10) was significantly lower than that in patients without sarcopenia (n = 62) (1-year overall survival rate; 56% versus 98%, resepctively) ($p < 0.001$). SMM worsened after LDLT and did not recover to preoperative levels until 1 year after LDLT. In contrast, HS recovered to preoperative levels at 6 months after LDLT following sharp decrease at 1 month after LDLT. According to preoperative sarcopenia, postoperative HS in patients without sarcopenia tended to be lower compared to patients with sarcopenia, while postoperative SMM did not differ between patients with sarcopenia and those without sarcopenia.
**Conclusion:** Prospective analysis clarified that pretransplant sarcopenia had negative impact on short-term survival after LDLT. The recovery of handgrip strength preceded that of SMM.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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TUESDAY, OCTOBER 18, 2016 09:00–17:00
**IBD II – POSTER EXHIBITION**

### P0788 SILVER NANOPARTICLES NANOAG1 AND NANOAG2 ATTENUATE EXPERIMENTAL COLITIS IN MICE THROUGH MODULATION OF COLONIC MICROBIOTA

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**Introduction:** The role of intestinal microbiota in inflammatory bowel disease (IBD) development and exacerbation has been widely studied, but is still poorly understood. Microbiota have thus become a potential pharmacological target in IBD therapy. Silver preparations are well known of their broad spectrum of antimicrobial and anti-inflammatory actions. The activity of silver nanoparticles depends on their size and shape, which affect the interaction with biological membranes in microbiota and the host, and the immune system of the host.
**Aims & Methods:** Aims: The aim of this study was to investigate the effect of newly developed silver nanoparticle aqueous suspensions varying in shape and size, NanoAg1 and NanoAg2 (spherical shape, 294 nm in diameter and irregular shape, 122 nm in diameter, respectively) in the mouse models of experimental colitis. Methods: NanoAg1 and NanoAg2 were synthesized by a one-step chemical reduction in aqueous medium with the involvement of tannic acid. UV-Vis spectroscopy and atomic force microscope microphotographs were made to confirm the size and the shape of nanoparticles. To assess the anti-inflammatory activity of tested compounds, semi-chronic mouse models of inflammation induced by DSS addition to drinking water and intracolonic (i.c.) administration of TNBS were used. Macroscopic score, ulcer score, colon length, weight and thickness, as well as, microscopic score were recorded. Moreover, in all experiments the level of myeloperoxidase (MPO) activity was determined as an indicator of neutrophil infiltration in the colonic tissue. The effect of silver nanoparticles on colonic microbiota was studied ex vivo by recording the number of total bacteria, *Escherichia coli*, *Lactobacillus species* and *Clostridium perfringens* in stool content.
**Results:** NanoAg1 and NanoAg2 (0.05 mg/dm$^3$, 100 μL/animal, i.c., once daily) significantly ameliorated colitis in DSS- and TNBS-induced mouse models of colonic inflammation, as indicated by reduced macroscopic, ulcer and microscopic scores. However, the anti-inflammatory effect was dependent on the shape and diameter of silver nanoparticles, as indicated by weaker effect of NanoAg1 than NanoAg2. The MPO activity was reduced after i.c. installation of NanoAg1 and NanoAg2. In addition, administration of NanoAg2, but no NanoAg1 modulated colonic microbiota, as indicated by reduced number of *E. coli* and *C. perfringens*, and increased number of *Lactobacillus* sp.
**Conclusion:** We propose a novel adjuvant therapeutic strategy to induce remission in IBD, based on the treatment with silver nanoparticle aqueous suspensions and modulation of colonic microbiota.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0789 MACROPHAGES BEHAVIOUR AGAINST ADHERENT AND INVASIVE E. COLI (AIEC) ISOLATED FROM CROHN'S DISEASE PATIENTS IN RELATION WITH HOST FACTORS SUSCEPTIBILITY

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**Introduction:** Crohn's disease (CD) is a chronic inflammatory bowel disease which altere quality of life, leads to significant disability, and slightly increased mortality rate. The pathophysiology of the CD remains imperfectly elucidated. The most recent hypothesis considered CD as resulting from an abnormal interaction between microbiota and host immune system influenced by genetics and environmental factors. Ileal lesions of CD patients are abnormally colonized by adherent-invasive *E. coli* (AIEC) able to survive in macrophage cell lines. The macrophages play a pivotal role in the elimination of pathogenic bacteria via autophagy which is one of the main pathways responsible for the elimination of intracellular bacteria and which play a key role in CD. We recently reported that macrophages from CD patients could have an impaired ability to restrict intracellular AIEC replication.
**Aims & Methods:** In the present study we aimed to understand why macrophages from CD patients have a deficient control regarding AIEC infection in searching a correlation between AIEC replication and several CD genetics polymorphisms especially those related to autophagy. Peripheral blood monocyte-derived macrophages (MDM) were obtained from 95 CD patients, 30 ulcerative colitis patients and 15 healthy volunteers, genotyped for ULK, XBP1, CYLD, USP40, LRRK2, NOD2, IRGM and ATG16L1 mutations. The numbers of intracellular bacteria were determined at 1 h and 10 h post-infection using gentamicin assay. Cytokine secretion was quantified by ELISA. Factors (including clinical factors, current therapies, CDAI, SCCAI, CRP, vitamin D and fecal calprotectin values, genetics polymorphisms...) associated with AIEC uptake/survival/replication were investigated using multivariate analysis.
**Results:** The bacteria uptake and ability to survive and replicate within MDM were significantly higher for AIEC reference strain LF82 comparatively to the non-pathogenic *E. coli* K-12 regardless macrophages origin. The AIEC uptake (1 h post-infection) within MDM did not differ according to MDM origin. The AIEC survival (10 h post-infection) within MDM from CD patients was higher than AIEC survival within MDM from UC patients and helathy volunteers ($p = 0.0019$). In multivariate analysis, AIEC survival within MDM from CD patients was positively correlated with IL1-$\beta$ secretion ($p < 0.0001$) and was decreased in the presence of ULK1 ($p = 0.046$) and XBP1 ($p = 0.014$) mutations. AIEC were able to replicate within MDM from CD patients but not within MDM from UC patients or healthy volunteers ($p < 0.001$). In multivariate analysis, AIEC intracellular replication was increased in CD patients with IRGM mutation ($p = 0.045$).
AIEC infection of MDM from CD patients induced an increased secretion of pro-inflammatory cytokines/chemokines IL-1$\beta$, IL-8, IL-6 and TNF-$\alpha$ compared to both basal secretion and K-12 infection.
**Conclusion:** ULK-1, XBP-1 and IRGM polymorphisms are implicated in macrophages deficiency to control intracellular AIEC replication leading to disordered inflammatory response. Our results highlighted the implication of Crohn's disease ULK-1, XBP-1 and IRGM polymorphisms in macrophages abnormalities which are suspected to account for some immunological defects associated with the development of Crohn's disease. Further work is required in Crohn's disease patients to phenotypically characterized MDM and to define how ULK-1, XBP-1 and IRGM could modulate AIEC uptake/survival/replication within MDM. This may lead to develop new therapeutic strategy based on manipulation of macrophage phenotype and on host-pathogen interaction in selected patients.
**Disclosure of Interest:** A. Buisson: Consulting for Abbvie and Takeda Lecture fees for MSD, Abbvie, Takeda, Ferring, Hospira, Vifor Pharma
All other authors have declared no conflicts of interest.

### P0790 THE EFFECT OF ORAL S1P RECEPTOR MODULATOR (FTY720) ON COMPLEMENT CASCADE AND NUMBER OF NORMAL STEM CELLS TRAFFICKING IN PERIPHERAL BLOOD IN A MURINE MODEL OF ULCERATIVE COLITIS

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**Introduction:** FTY720 (fingolimod) is oral sphingosine-1-phosphate (S1P) receptor agonist with documented immunomodulatory function. FTY720 was shown to be clinically effective in the treatment of multiple sclerosis and colitis in IL-10-deficient and $CD4^+CD62L^+$ cell-transfer animal model. Another S1P receptor modulator (RPC1063) was effective in induction of clinical remission and mucosal healing in TOUCHSTONE (1) study in patients with moderate to severe ulcerative colitis (UC). Based on these results S1P receptor modulators have been proposed as novel therapeutic option for the treatment of UC. We have previously documented that the number of normal stem cells (SCs) circulating in peripheral blood increases in patients with inflammatory bowel disease (IBD) (2) and reported that these SCs could be implicated in tissue/organ regeneration (3,4). However the effect of S1P modulators on normal SCs mobilization in UC is currently unknown.
**Aims & Methods:** In the current study we investigated the effect of FTY720 on components of complement cascade and number of normal SCs mobilized into peripheral blood (PB) in UC. Male, 8-week-old, C57BL/6J mice were administered FTY20 after induction of colitis with dextran sulfate (DSS). The disease activity index (DAI) was monitored daily by measuring the body weight, stool consistency and rectal bleeding. Bone marrow (BM) derived SCs expressing Sca-1, CD45, c-kit and lack of lineage specific markers were identified by fluorescence-activated cell sorting (FACS) analysis. Plasma levels of complement cleavage fragments (C5a), intestinal fatty acid binding protein (I-FABP) and vascular endothelial growth factor (VEGF) were measured by ELISA. S1P plasma levels were measured by liquid chromatography. BM-derived PB MNCs were tested for their ability to form granulocyte-monocyte (CFU-GM) and erythroid (BFU-E) colonies. Histopathological analysis of intestinal tissue specimens was performed.
**Results:** FTY20 administration was followed by decrease in disease activity index (DAI) of mice with DSS colitis. The administration of FTY720 resulted in reduced egress from BM into PB of all populations of SCs studied. FTY720 administration was associated with lower levels of serum S1P, decreased expression of plasma I-FABP (marker of intestinal permeability) and VEGF vascular markers. The plasma levels of complement cascade (CC) fragments were not manipulated by FTY720 treatment. The intestinal gross pathology revealed less advanced damage of epithelial cells and increased vessel formation in intestines of FTY20 treated animals.

**Conclusion:** Beneficial effect of FTY720 administration in murine model of DSS colitis is associated with reduced egress of inflammatory cells into PB, decrease in intestinal permeability and increase in angiogenesis. Decrease in mobilization and trafficking of SCs in PB in UC after FTY720 treatment is also observed.
**Disclosure of Interest:** W.M. Marlicz: This study was supported by European Union grant POIG.01.01.02–00-109/09
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All other authors have declared no conflicts of interest.

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### P0791 MICROBIAL COMPOSITION AND FUNCTION ARE ASSOCIATED WITH ILEAL POUCH SYMPTOMS INDEPENDENTLY OF INFLAMMATION

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**Introduction:** Pouchitis is a common complication after ileal pouch–anal anastomosis (IPAA). However, there is a poor correlation between symptoms and endoscopic appearance and many pouch patients can have debilitating symptoms in the absence of overt inflammation. It remains unknown whether these clinical symptoms are independently associated with the microbiota.
**Aims & Methods:** The objective of this work was to examine if the clinical components of the pouch activity scoring systems are associated with microbiota. Pouch biopsies from 202 patients (50%male) post IPAA were included. Illumina MiSeq sequences were processed using QIIME pipeline v1.9. Microbiome functions were imputed using Picrust software. Clinical phenotyping was performed and patients were classified using both clinical and endoscopic components of the Pouch Activity Scale. Associations were performed using linear regression adjusting for age, gender and antibiotic use, first in patient with endoscopic inflammation ($n = 99$) and second in patient with no inflammation ($n = 103$). Scoring for symptoms examined 24 h stool frequency, urgency, incontinence and rectal bleeding as described by PAI score
**Results:** In the absence of inflammation, presence of symptoms was associated with Firmicutes ($q < 0.04$) and 24 h stool frequency was associated with an undefined Clostridiales species among others ($10^{-6} < q < 10^{-5}$). In the inflamed individuals, 24 h stool frequency was associated with Bacillales ($q < 0.02$) and with an unknown species of Lachnospiraceae ($q < 0.05$). Picrust analysis in inflamed groups showed that 24 h stool frequency was associated with synthesis/biofilm formation ($q < 0.05$).
**Conclusion:** These findings indicate that in patients with an IPAA, the composition of mucosa associated microbiota of the pouch contribute to clinical symptoms, in particular stool frequency, independently of endoscopic disease activity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0792 PHARMACOKINETICS AND PHARMACODYNAMICS FOLLOWING ORAL ADMINISTRATION OF PTG-100, A PEPTIDE ANTAGONIST OF INTEGRIN A4B7

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**Introduction:** The $\alpha4\beta7$ integrin is a clinically validated target in inflammatory bowel disease (IBD) as reflected by the FDA-approval of the humanized monoclonal antibody vedolizumab (Entyvio®) for the treatment of moderate-to-severe ulcerative colitis and Crohn's disease. Vedolizumab binds to $\alpha4\beta7$ on circulating memory/effector T cells in the blood and blocks their homing to intestinal tissues that express the ligand MAdCAM-1. PTG-100 is a novel oral $\alpha4\beta7$ antagonist peptide that has minimal systemic absorption and is therefore largely restricted to the gut tissues. PTG-100 is currently in a Phase 1 study in normal healthy volunteers and will be developed for patients with ulcerative colitis. The aim of these studies was to characterize the pharmacokinetic (PK) properties and pharmacodynamic (PD) activities of PTG-100 in mice and cynomolgus monkeys to support the clinical development of PTG-100.
**Aims & Methods:** We conducted PK and PD studies in mice, rats, and cynomolgus monkeys, with peptide concentrations measured by mass spectrometry. We measured $\alpha4\beta7^+$ memory T cell receptor occupancy, surface expression, and cell numbers in whole blood using Fluorescence Activated Cell Sorting (FACS) to assess PD activity. Cell trafficking in blood and gut lymphoid tissues was measured by FACS or immunohistochemistry (IHC).
**Results:** Oral dosing of PTG-100 in normal or dextran sodium sulfate (DSS)-treated mice and rats showed a dose-dependent exposure in the small intestine, colon, and Peyer's Patches (PP), with very low exposure in the blood and urine. Oral bioavailability (%F) in mice was $<0.5$, indicating that PTG-100 is largely gut restricted. PK studies in cynomolgus (cyno) monkeys showed that oral bioavailability of PTG-100 was $<0.5$ and up to 40% in feces. Daily dosing with PTG-100 in murine DSS colitis models showed a dose-dependent reduction in $CD4^+$ $CD44^{high}$ $CD45RB^{low}$ $\beta7^+$ T cells in the mesenteric lymph node (MLN) and PP, and concomitant increase in the spleen and blood as measured by FACS. There was also a strong reduction of $\beta7^+$ cell and polymorphonuclear cell infiltration into lamina propria lesions of the distal colon. At these pharmacologically active doses, $\alpha4\beta7$ receptor occupancy (RO) in the blood, MLN and PP ranged from 46–81% at 4 h post dose. PTG-100 also induced a strong downregulation of $\alpha4\beta7$ integrin surface expression on $CD4^+$ effector T cells in murine blood. In normal cynos, once daily oral dosing of PTG-100 resulted in a dose-dependent increase in RO of memory T cells and an increase of $\alpha4\beta7$ memory $CD4^+$ T cell numbers in the peripheral blood.
**Conclusion:** PTG-100 is a novel oral $\alpha4\beta7$-selective antagonist being developed for the treatment of patients with ulcerative colitis. It is largely gut restricted and alters the trafficking of gut-homing T cells in mice and cynomolgus monkeys. These studies showed that PTG-100 induced downregulation of $\alpha4\beta7$ expression on memory T cells in the blood may be an additional and important mechanism for inhibiting T cell trafficking. Together, these results support clinical development of PTG-100.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0793 ENDOPLASMIC RETICULUM STRESS ENHANCES THE RELEASE OF SERINE PROTEASES BY EPITHELIAL CELLS ALTERING THE INTESTINAL BARRIER FUNCTION

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**Introduction:** The pathophysiology of ulcerative colitis (UC) is characterized by an excessive induction of the endoplasmic reticulum stress (ERS) in epithelial cells (IEC) of colonic mucosa. Moreover, an excessive proteolytic activity has been described in IEC in course of UC.
**Aims & Methods:** We aimed to investigate the impact of the ERS on trypsin-like activity (TLA) in enterocytes and goblet cells, and its reflection on the intestinal barrier function. Human cell lines Caco2 (enterocyte) and HT29MTX (Goblet cell) were stimulated with Thapsigargin (10 µg/mL) and Tunicamycin (20 µg/mL) to induce ERS. TLA in the supernatant was analyzed at 2, 4, 6 and 24 hours and mRNA expression of serine proteases from cell lysates was analyzed at 6 and 24 hours. The impact of ERS on intestinal barrier function was evaluated by measuring the paracellular permeability (transwell system), IL8 secretion and the mRNA expression of anti-microbial peptides (AMP). To assess the role of the serine proteases released by ERS on the intestinal barrier function, human cells lines were treated with serine proteases inhibitors (AESBF 20uM and Leupeptin 50uM). In addition, the involvement of Proteases Activated Receptor (PAR) -1, -2, -3 and -4 after ERS induction was evaluated by measuring their mRNA expression in the presence or absence of antagonists.
**Results:** Inducing ERS by Thapsigargin or Tunicamycin enhanced the secretion of Trypsin-like proteases by Caco-2 and HT29MTX cells at 2, 4, and 6 hours, but not at 24 hours, probably due to inducer depletion. This activity was prominent in the apical side of IEC. At 6 and 24 hours, the expression of the three main Trypsin-like proteases (PRSS1, 2 and 3) mRNA was increased in IEC. Next, we have evidenced that ERS increased permeability, the release of IL-8 at apical and basolateral side of the epithelium and mRNA expression of the Resistin Like Molecule $\beta$ (RLM $\beta$), known as a proliferative IEC and AMP molecule. Serine protease inhibitors inhibited the ERS-increased permeability and RLM$\beta$ mRNA overexpression, while they aggravated IL-8 secretion. In addition, protease inhibitors also suppressed the increased mRNA expressions of PRSS1, 2 and 3. Lastly, ERS increased the PAR-2, -3 and -4 mRNA level while it downregulated PAR-1 expression.
**Conclusion:** Our results show that ERS induces the release of Trypsin-like activity in the apical side of enterocytes and muco-secreting cells. The deregulation of proteases leads to destabilization of the epithelium homeostasis. Although PAR-1 expression was downregulated by ERS, it mediated the impact of serine proteases released by ERS to alter the IBF. These results evidence a crosstalk between ERS and serine proteolytic activity to destabilize the IBF, playing a potential role in UC development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0794 EFFECTS OF HUMAN AMNION-DERIVED MESENCHYMAL STEM CELL TRANSPLANTATION AND CONDITIONED MEDIUM ENEMA IN RATS WITH TRINITROBENZENE SULFONIC ACID-INDUCED COLITIS

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**Introduction:** Mesenchymal stem cells (MSCs) have been reported to be a valuable cell source in regenerative medicine, and bone marrow represents a major source of MSCs. Recently, it has been shown that MSC can be easily isolated from human amnion, which is generally discarded after delivery, and a large amount of cells can be obtained. We have previously reported that intravenous administration of human amnion-derived MSCs (hAMSCs) provided significant improvement in rats with colitis induced by dextran sulfate sodium or g-irradiation. In addition, conditioned medium (CM) obtained from MSCs contains a variety of humoral factors to improve damaged tissues. In this study, we investigated the effects of hAMSCs and CM in rats with 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis.
**Aims & Methods:** hAMSCs were isolated and expanded by digestion with collagenase, followed by culturing in uncoated plastic dishes. CM was collected by culturing subconfluent hAMSCs with serum-free MEMa for 48 hrs. CM gel was prepared by mixing CM with 2% carboxymethyl cellulose. On day 0, 200 $\mu$l of TNBS (15 mg/rat) in 30% ethanol was intrarectally administered to the ten-week-old male Sprague-Dawley (SD) rats. One-million hAMSCs were intravenously administered 3 hrs after TNBS treatment, and rats were sacrificed on day 7 for histological examination and quantitative PCR. In another experiment, 400 $\mu$l of CM gel was intrarectally administered 3 hrs after TNBS treatment, and day 1 and day 2.
**Results:** hAMSC transplantation and CM gel enema significantly improved the endoscopical score, and tended to improve the histological score. Quantitative PCR demonstrated that the expression levels of TNF-$\alpha$, CXCL1 and CCL2 tended to be decreased by hAMSC transplantation and CM gel enema. Infiltrations of CD68-positive macrophages and myeloperoxidase-positive neutrophils were significantly decreased by hAMSC transplantation and CM gel enema.
**Conclusion:** Transplantation of hAMSCs and CM gel enema provided significant improvement in rats with colitis induced by TNBS. hAMSCs or CM from hAMSCs may be new therapeutic strategies inflammatory bowel disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0795 TERTIARY LYMPHOID ORGANS IN GUT MUCOSA OF NEWLY DIAGNOSED, UNTREATED INFLAMMATORY BOWEL DISEASE PATIENTS

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**Introduction:** There is recent evidence of increased naïve and central memory T lymphocytes ($T_N$ and $T_{CM}$) mucosal infiltration of the inflamed gut in Inflammatory Bowel Disease (IBD), while $T_N$ and $T_{CM}$ cells were thought to migrate exclusively to secondary lymphoid organs (SLOs). Ectopic formation of tertiary lymphoid organs (TLOs) containing peripheral lymph node adressin $(PNAd)^+$ high endothelial venules (HEVs) might explain the homing of these lymphocytes to the gut, as PNAd is the ligand of L-selectin which is expressed on $T_N$ and $T_{CM}$ lymphocytes.
**Aims & Methods:** The aim of this study was to investigate the presence of PNAd expressing HEVs and TLOs in the inflamed intestinal mucosa of newly diagnosed, untreated, IBD patients in relation to the presence of $T_N$ and $T_{CM}$ lymphocytes. Thirty-nine newly diagnosed, untreated IBD patients and eight healthy controls were prospectively included. Intestinal biopsy samples were analysed by immunohistochemistry for blood vessels (CD31) and PNAd expression (MECA-79), the density of MECA-$79^+$ vessels was calculated and the presence of lymphoid follicles was assessed. Different lymphocytes subsets in the tissue samples were identified by flowcytometric immunophenotyping, including $T_N$ ($CD45RA^+CD27^+$), $T_{CM}$ ($CD45RA^-CD27^+$) and effector memory T cells ($CD45RA^-CD27^-$).
**Results:** A statistically significant higher number of extra-follicular $PNAd^+$ vessels were found in the inflamed colon of patients with ulcerative colitis (median density of 3.05 $PNAd^+$ vessels/$mm^2$ (IQR 0–6.39)) and ileum of patients with Crohn's disease (median density of 1.40 $PNAd^+$ vessels/$mm^2$ (IQR 0–4.34)) compared with healthy controls (median density of colon: 0 $PNAD^+$ vessels/$mm^2$ (IQR 0–0, $p = 0.033$) and ileum: 0 $PNAd^+$ vessels/$mm^2$ (IQR 0–0.50, $p = 0.033$)). The heterogeneity of extra-follicular $PNAd^+$ vessels in IBD patients allowed classification in two different groups: $HEV^{high}$ and $HEV^{low}$. A high density of $PNAd^+$ HEV-like vessels was associated with increased numbers of $T_N$ and $T_{CM}$ in the inflamed gut mucosa (median 87% (IQR 82–93%) of total T cell population), compared with the inflamed mucosa of patients from the $HEV^{low}$ group (58% (IQR 38–81%) $p = 0.003$). The number of colonic follicles was higher in $HEV^{high}$ patients (median 0.54/$mm^2$ (IQR 0.28–0.84)) when compared with $HEV^{low}$ patients (median 0.25/$mm^2$ (IQR 0.08–0.45) $p = 0.031$) and controls (0.31/$mm^2$ (IQR 0.23–0.45) $p = 0.043$).
**Conclusion:** For the first time, evidence has been delivered of extra-follicular HEV-like vessels and TLOs, strongly associated with $T_N$ and $T_{CM}$ cell mucosal infiltration, in a subgroup of newly diagnosed IBD patients. Different T cell migration phenotypes based on TLO formation in the early phase of IBD might allow risk-stratification of patients and enable more effective, individualized treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0796 TOLL-LIKE RECEPTOR 9 MODIFIES INTESTINAL SEROTONERGIC SYSTEM

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**Introduction:** Toll-like receptor 9 (TLR9) is expressed in intestinal epithelial cells, which recognize microbiota developing different responses [1]. Several studies have shown that TLR9 seems to be involved in Inflammatory Bowel Diseases (IBD) due to an inappropriate defensive response against microorganisms [2]. Moreover, intestinal serotonergic system is also altered in IBD, where extracellular serotonin (5–HT) levels are increased [3]. 5-HT bioavailability is mainly regulated by the serotonin transporter (SERT), expressed in enterocytes [4].
**Aims & Methods:** The aim of the present study was to analyse whether TLR9 activation affects SERT expression and activity, and expression of other elements from the serotonergic system (TPH1, TPH2 and 5-HT receptors). Human enterocyte-like Caco-2 cells, and ileum and colon from $TLR9^{-/-}$ mice and Dextran Sulphate Sodium (DSS) mouse colitis model were used as experimental models. mRNA expression was determined by RT-qPCR, and protein expression by western blot.
**Results:** TLR9 activation in Caco-2 cells decreased SERT mRNA and protein expression. TLR9 activation also reduced SERT activity by different intracellular pathways, depending on activation period. Indeed, TLR9 long-time activation altered 5-HT uptake through ERK pathway, whereas short-time activation modified SERT by p38/MAPK pathway. Moreover, 5-HT addition to culture media increased TLR9 protein expression in the brush-border membrane of Caco-2 cells. In $TLR9^{-/-}$ mice were observed different expression patterns. SERT was not modified in ileum, but increased in colon. TPH1 was increased in ileum, and TPH2, in colon. Regarding 5-HT receptors, 5HT2A, 5-HT2B, and 5-HT3 were increased in ileum; however, 5-HT1A, 5-HT2A and 5-HT4 were increased in colon. In both ileum and colon of DSS mice, TLR9 and 5-HT7 mRNA expression were increased, whereas SERT expression was diminished.
**Conclusion:** Our results suggest that TLR9 modulates intestinal serotonergic system. Indeed, TLR9 activation decreases SERT function and expression by different pathways. In part, this is corroborated by the decreased expression of SERT in colon of TLR9 knockout mice and altered 5-HT receptors expression. Finally, SERT and TLR9 are inversely disturbed in DSS mice colitis model.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0797 ASSOCIATION OF BACTEROIDETES WITH ENDOSCOPIC ACTIVITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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**Introduction:** The role of gut microbiota on the etiopathogenesis of IBD, both Crohn's disease (CD) and ulcerative colitis (UC), is not well known. Most studies of human gut microbiota rely on the non-invasive collection of stool samples. However, the analysis of the fecal microbiota may not reflect the role of the mucosa-associated microbes. Mucosa-associated germs live in close proximity to the intestinal epithelium and are in contact with the cells of the innate immune system directly involved in the inflammatory response
**Aims & Methods:** Aim of this study was to investigate the genotypes of Bacteroidetes microbiota from colon biopsies of IBD patients and to determine their relationship with the endoscopic activity of the disease. Methods:
A single-center, observational cross-sectional study was designed. Consecutive patients with Crohn's disease (CD) and ulcerative colitis (UC) who attended the Endoscopy Unit of Santiago de Compostela for colonoscopy were included. Colonic biopsies were taken to characterize microbiota by using a restriction fragment length polymorphism (RFLP) analysis on PCR products targeting the 16SrRNA genes of Bacteroidetes digested with HinfI, PciI, DpnII and AciI. Inactive UC was defined as a Mayo endoscopic score of 0. Inactive CD was defined as a SES-CD $<= 2$. The association of endoscopic activity with demographic (gender, age and smoking habits) and analytical (VSG, PCR and platelets) factors was also evaluated. The results were expressed as prevalence and analyzed using logistic regression.
**Results:** 52 consecutive IBD patients (28 CD and 24 UC) were included. 33 patients showed endoscopic activity of the disease (20 CDa and 13 UCa). A total of eight genotypes of Bacteroidetes called N1, C1-C5, CB 10 and CB13 were detected. N1 is probably a strain of Bacteroides dorei, and C1 and C2 B.vulgaris strains. While the presence of N1 and C1 genotypes was consistent in patients with active and inactive IBD, the percentage of C4 genotypes in patients with UCa and CDa was very high (81.8%) compared to patients without activity (36.8%) ($p = 0.001$). C3 genotype was observed in 4/19 inactive IBD patients and in 12/33 of active IBD patients ($p = 0.24$). Other genotypes were found sporadically in IBD biopsies. No differences were observed between the genotype of patients with CD or UC. After multivariate analysis, C4 genotype in colon biopsies was associated with endoscopic activity of the disease (OR 8.58, 95%CI 2.16 to 34.08) ($p = 0.02$).
**Conclusion:** The presence of genotype C4 of Bacteroidetes is associated with the endoscopic activity of IBD, both CD and UC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0798 GENETIC DIFFERENCES IN THE OUTER MEMBRANE PROTEINS SEQUENCE AMONG COMMENSAL AND ADHERENT-INVASIVE E. COLI STRAINS

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**Introduction:** Outer Membrane Proteins (OMPs) usually play a role in antibiotic resistance of *Escherichia coli* by making the bacterium less permeable when decreased expression or variations in pore conformation occur. Moreover, OmpA has been implicated in the invasion ability of Adherent Invasive E. coli (AIEC) pathotype by binding the receptor Gp96, overexpressed in Crohn's disease patients (1). An indirect role in AIEC adhesion and invasion has also been suggested for OmpC (2).
**Aims & Methods:** The aim of this study was to identify gene mutational patterns in OMPs among a collection of AIEC and non-AIEC strains, to determine possible associations between them and antibiotic resistance or AIEC pathogenicity. The genes of OMPs ompA, ompC and ompF were sequenced from a collection of 22 AIEC and 29 non-AIEC strains tested for resistance to 27 antimicrobials. For comparison, genes from AIEC, UPEC, MNEC, APEC, EAEC, EHEC, ETEC and commensal strains were retrieved from GenBank. Phylogenetic tree analysis and allele identification was performed using MEGA5 (Neighbour-joining, Poisson correction distance and 10,000 bootstrap replicates). The genetic differences were annotated using as reference the LF82 strain. Then, they were analysed statistically according to AIEC pathotype, phylogroup origin, and antibiotic resistance by the $\chi^2$ test and non-parametric tests were used to evaluate amino acid variability regarding the invasion index.
**Results:** The OmpA protein sequence shared a 93.2% of similarity among the strain collection. For OmpF and OmpC was 92.4% and 83.4%, respectively. Phylogenetic tree analysis clustered the strains in 9 groups for OmpA, 2 for OmpF and 12 for OmpC. Most of the variation occurred in the extracellular loops, a total of 22 amino acid changes in OmpA, 28 in OmpF and 61 in OmpC were found. The distribution of amino acid variants was similar between AIEC and non-AIEC. However, despite not reaching statistical significance, higher invasion indices were observed in strains with specific amino acids changes in position 114 of the OmpA sequence, in position 115 of OmpF and in different positions across OmpC extracellular loops 2, 5 and 7. Amino acid variants of each porin (3 of the variable positions of OmpA, 2 of OmpF and 16 of OmpC) correlated with phylogroup origin of the strains, being A phylogroup the one resembling more to B1 and B2 to D ($p < 0.05$). Resistance to $\beta$-lactams amoxicillin-clavulanate and ticarcillin-clavulanate was more frequently observed in strains with P131 OmpA variant ($p = 0.024$), tetracycline and doxycylin resistance with OmpF variations in P264_274 ($p = 0.010$) and streptomycin resistance with OmpC P191 and P220 variants ($p < 0.05$).
**Conclusion:** In conclusion, no amino acid changes in OmpA, OmpF and OmpC were found distributed specifically and across all AIEC, but some amino acid variants correlated with higher invasion ability what could depict pathoadaptative mutations associated with virulence. Additional molecular studies are needed to evaluate the finding of site-specific mutants presenting particular resistance phenotypes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0799 ANTIBIOTICS-MEDIATED INCREASE IN LARGE INTESTINAL PROTEASE ACTIVITY IS ASSOCIATED WITH IMPAIRED INTESTINAL BARRIER FUNCTIONS AND AGGRAVATION OF SPONTANEOUS COLITIS

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**Introduction:** Early exposure to antibiotics (AB) has been associated with increased risk for later development of inflammatory bowel diseases (IBD) but the causal relevance and pathophysiological mechanisms are unknown. Specific AB treatments induce a major increase of the large intestinal protease activity (liPA) via the elimination of bacteria that mediate the physiological inactivation of pancreatic proteases in the large intestine.
**Aims & Methods:** We hypothesized that the AB-mediated rapid increase in liPA may impair the large intestinal barrier and promote the development of chronic inflammation. In order to investigate this hypothesis, we treated wildtype (WT) and interleukin 10 deficient (IL10-/-) mice with vancomycin/metronidazole (V/M) and investigated the impact of this AB therapy on the liPA, the intestinal barrier function and the subsequent susceptibility towards dextran sodium sulfate (DSS)-induced and spontaneous colitis.
**Results:** V/M-mediated elimination of anti-proteolytic bacteria in the large intestinal ecosystem resulted in a rise of large intestinal pancreatic trypsin (~20x) and liPA (~5–10x), being comparable to the levels observed in GF mice. Transwell and Ussing chamber analyses using large intestinal epithelial cells or cecal tissue revealed that the high proteolytic activity in cecal supernatants (CS) from V/M-treated or GF mice significantly impaired the epithelial barrier function in a serine protease dependent way. In WT and IL10-/- mice, the acute V/M-mediated increase in liPA was associated with impaired large intestinal barrier functions (Ussing chamber) and increased translocation of orally applied FITC dextran (4 kDa) to the systemic circulation. Importantly, oral co-administration of a serine protease inhibitor, AEBSF, maintained normal intestinal barrier functions in V/M-treated WT mice. Repeated short term V/M treatments of WT mice ($2 \times 7$ days, at 4 and 8 weeks of age) resulted in chronically increased liPA but did not affect later susceptibility towards DSS-induced colitis (at 12 weeks). However, analogously V/M-treated IL10-/- mice showed accelerated development of chronic colitis, systemic inflammation and large intestinal tumor formation.
**Conclusion:** V/M treatment results in a rapid and major increase in liPA which is detrimental to the intestinal barrier. Pulsed V/M treatments mediated a chronic increase in liPA as well as accelerated colitis development in IBD susceptible mice. These findings demonstrate that specific AB therapies can indeed promote the development of IBD in disease susceptible organisms and indicate that the increase in liPA may contribute to this long-term adverse effect.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0800 OXIDATIVE STRESS PARAMETERS FOR THE DISEASE ACTIVITY EVALUATION IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** Neutrophils dependent oxidative stress (OS) in the intestinal mucosa plays an important role in ulcerative colitis (UC) disease. Several antioxidants inhibit the inflammatory responses in intestinal tracts system. Therefore, we investigated reactive oxygen species (ROS) and antioxidants levels in tissue specimens and their correlation with disease activity.

**Aims & Methods:** In total, 44 UC patients (M/F 23/21, mean age $41.2 \pm 11.8$) were compared with 33 controls (M/F 18/15, mean age $48.23 \pm 15.12$). Clinical disease activity was estimated according to Truelove–Witts Index values $<150$, 150–220, and $>220$ corresponded to mild, moderate, and severe, respectively. OS was estimated based on malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPX), and myeloperoxidase (MPO) levels in tissue specimens using the thiobarbituric acid-trichloroaceticacid assay for MDA-phenyltetrazolium chloride assay for SOD, method of Paglia and Valentine for GPX, and tetramethyl benzidin assay for MPO measurement. Chi-square test, Student's t-test, Mann–Whitney test, multivariate regression analysis, and the area under receiver operating characteristic (ROC) curve were used for statistical analysis

**Results:** In controls, MDA levels correlated positively with GPX, MPO, and SOD levels ($r = 0.68$, $p = 0.02$; $r = 0.72$, $p = 0.02$; $r = 0.42$, $p = 0.03$, respectively). MDA level of patients with mild AI correlated positively with GPX and SOD levels ($r = 0.73$, $p = 0.01$ and $r = 0.82$, $p = 0.01$, respectively). Patients with mild and moderate AI had similar MDA levels as the controls. Patients with severe AI had significantly higher MDA and MPO levels than the controls did ($p = 0.03$ and 0.004, respectively), but in patients with high AI, MDA levels correlated inversely with the GPX and SOD levels ($r = -0.79$, $p = 0.01$ and $r = -0.68$, $p = 0.03$, respectively). The ROC curves revealed statistically significant discriminative power of MDA and MPO levels for high AI (AUROC = 0.69 and 0.58, respectively). Tissue MDA ($B = 0.22$, $p = 0.006$), and MPO levels ($B = 1.48$, $p = 0.03$), were independently associated with high AI. Increased MDA (OR 1.48; %95 CI, 1.08–2.16, $p = 0.04$) was risk factor for disease severity and increase of SOD- and GPX activity had preventive effect against high AI (OR 0.008; %95 CI, 0.001–0.98, $p = 0.04$ and OR 0.006; %95 CI, 0.02–0.67, $p = 0.045$, respectively).

**Conclusion:** Our findings show that UC patients with enhanced oxidative stress and subsequent depletion of antioxidant capacity have increased risk for severe clinical activity. Therefore, therapeutic interventions with antioxidant agents should be considered for the treatment in UC patients with high clinical activity index

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0801 AQUAPORIN EXPRESSION AND LOCALIZATION IN COLONIC BIOPSIES FROM COLLAGENOUS COLITIS PATIENTS

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**Introduction:** Collagenous colitis (CC) is an inflammatory bowel disease and common cause for watery diarrhoea. The diarrhoeal mechanisms in CC are poorly understood as well as the mode of action how budesonide effectively reduces stool frequency and improves stool consistency. Aquaporins are water channels responsible for absorption and water balance in the colon as well as water homeostasis inside cells. We therefore investigated aquaporins in colonic biopsies of CC patients with active disease and in clinical remission under budesonide therapy.

**Aims & Methods:** The aquaporin expression was assessed using qPCR on colonic biopsies. The aquaporins investigated were AQP1, AQP3, AQP4, AQP6, AQP7, AQP8, AQP9, AQP10 and AQP11. We also investigated the sodium/hydrogen exchanger 1 (NHE1).

**Results:** qPCR analysis of the colonic biopsies revealed a significant decrease in the mRNA expression of AQP1, AQP8, AQP11 and NHE1 in CC-patients compared to healthy controls. For AQP1 and AQP11 there were, however, no significant differences observed during budesonide treatment, compared to controls. We observed a significant increase in the expressions of AQP8 and NHE1 within the patient group during treatment. The clinical improvement seen in CC patients during treatment associates with restoration of AQPs expression.

**Conclusion:** CC patients showed a decreased expression level of AQP1, 8, 11 and NHE1 compared to healthy controls. During budesonide treatment the expression was re-established for AQP1 and 11 and significantly increased for AQP8 and NHE1 indicating an involvement of AQPs in CC. This is to our knowledge the first observation of AQP dysregulation in CC patients.

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All other authors have declared no conflicts of interest.

## P0802 ALTERED HUMAN DENDRITIC CELL PHENOTYPE AND SUBSET COMPOSITION IN THE BLOOD AND GASTROINTESTINAL TRACT OF ULCERATIVE COLITIS PATIENTS

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**Introduction:** Dendritic cells (DC), the most potent antigen presenting cells, determine the outcome (pro-inflammatory/tolerogenic) of antigen-specific adaptive immune responses. In the gastrointestinal tract, DC promote the mechanisms of immune tolerance towards the nutrients and the commensals while initiate immune responses against invading pathogens. Changes in their immunity/tolerance balance have been related with the development of inflammatory bowel diseases, including ulcerative colitis (UC).

**Aims & Methods:** Our aim was to characterize human DC (both circulating and intestinal) from endoscopically active UC patients and healthy controls. To that end, we performed a prospective, single centre study were intestinal biopsies were obtained from the inflamed colon and non-inflamed terminal ileum (TI) from UC patients. The colon and TI from non-inflamed healthy controls without autoimmune diseases, infections or malignancies were also sampled. Blood samples were obtained from the same patients/controls on the same day of the colonoscopy. All samples were immediately processed in the laboratory and characterized by flow cytometry.

**Results:** Human intestinal DC were identified within singlet viable $CD45^+$ cells as $HLA\text{-}DR^+CD11c^+CD14^-CD64^-$ and divided into subsets based on the expression of CD103 and SIRP$\alpha$. $CD103^-SIRP\alpha^+$ DC were the main intestinal subset and together with $CD103^+SIRP\alpha^+$ DC were $CD1c^+ILT3^+$. CCR2 was expressed in all $CD103^-SIRP\alpha^+$ DC with expression being variable on the $CD103^+SIRP\alpha^+$ subset, where it was inversely correlated with CD103 expression. $CD103^+SIRP\alpha^-$ DC constituted a minor subset and were $CD141^+ILT3^-CCR2^-$. Circulating DC were identified within the $HLA\text{-}DR^+CD14^-CD16^-CD19^-$ fraction as plasmacytoid (pDC, $CD123^+$) and myeloid (mDC, $CD11c^+$), being the later divided into mDC1 ($CD1c^+$) and mDC2 ($CD141^+$). mDC1 and pDC were $SIRP\alpha^+ILT3^+CCR2^+$ while mDC2 were $SIRP\alpha^-ILT3^-CCR2^-$. $CD1c^+$mDC (but not pDC or $CD141^+$mDC) were recruited in a CCR2-deppedent manner by the human colon before they subsequently up-regualted CD103 and down-regulated CCR2 expression in time. In UC patients, the numbers of intestinal $CD103^+SIRP\alpha^+$ DC were reduced. CCR2 expression was lower in both $CD103^+SIRP\alpha^+$ and $CD103^-SIRP\alpha^+$ subsets while HLA-DR intensity was also lower in all intestinal DC subsets. Such differences were indeed observed in both the inflamed colon and the non-inflamed (TI) tissue from UC patients compared with the matched tissue from the healthy controls with no differences between the inflamed and non-inflamed areas in UC patients. Circulating mDC1, mDC2 and pDC from UC patients also had lower HLA-DR expression in comparison with healthy controls.

**Conclusion:** Human intestinal DC subset composition and their phenotype are altered in both inflamed (colon) and non-inflamed (TI) intestinal segments in UC patients as well as in their circulating counterparts compared to healthy controls. Future studies will determine whether such differences are also resembled into a different functionality and should identify the mechanisms responsible for such differences.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0803 THE ROLE OF PLATELETS IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** Inflammatory Bowel Disease (IBD) is a chronic relapsing inflammatory disorder of the GI tract, thought to be caused by an uncontrolled immune response to commensal gut bacteria in genetically susceptible individuals. Patients with IBD have higher platelet counts and an increased risk of thrombosis than matched controls. Retrospective reviews have noted improvements in disease activity among patients taking antiplatelet therapy, and murine models have highlighted that Clopidogrel confers protection against mucosal damage. It is therefore possible that platelets play an active role in the disease pathogenesis through interaction with a plethora of immune cells.

**Aims & Methods:** Patients with Crohn's Disease undergoing therapeutic resections at Queen Elizabeth Hospital, Birmingham, donated tissue sections from both macroscopically active and non-active diseased regions. Matched blood samples were taken for Flow Cytometric analysis of activated platelets. Immunohistochemical staining to detect the presence of endogenous platelets within diseased samples, and functional adhesion assays were used to elicit the key integrins involved in platelet-immune cell interactions.

**Results:** Patients with Crohn's Disease had a significant decrease in the percentage of activated platelets compared to controls ($P < 0.02$), measured using percentage of P-Selectin positive platelets. The hypothesis that populations of activated platelets undergo sequestration within diseased bowel was supported by immunochemical staining. Immunohistochemical staining highlighted the

presence of Podoplanin-positive structures, likely to be macrophages, within diseased bowel, highlighting the importance of the podoplanin-CLEC-2 interactions in immune cell recruitment. Functional adhesion assays have highlighted key roles for P-Selectin in the interaction between platelets and immune cells.
**Conclusion:** These interactions show promise as novel therapeutic targets in the management of Inflammatory Bowel Disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0804 LOSS OF PRDX6 AMELIORATES DSS-INDUCED ACUTE AND CHRONIC COLITIS

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**Background:** An imbalance between cellular antioxidant defense system(s) and reactive oxygen species (ROS)-driven oxidative stress has been implicated in the pathogenesis of inflammatory bowel disease (IBD). Peroxiredoxin (Prdx) 6, a protective protein with GSH peroxidase and acidic calcium-independent phospholipase A2 activities, maintains an appropriate redox balance by clearing ROS and thereby optimizing gene regulation.
**Aims:** We therefore hypothesized that loss of Prdx6 would lead to enhanced susceptibility to DSS induced acute and chronic intestinal inflammation.
**Design:** To investigate the impact of Prdx6 in intestinal inflammation, we used wild type (WT), Prdx6 knock-out mice ($Prdx6^{-/-}$) and transgenic mice ($Prdx6^{+/+}$), expressing a constitutively active form of Prdx6. Acute and chronic colitis was induced by dextran sulfate sodium (DSS) in WT, $Prdx6^{-/-}$, and $Prdx6^{+/+}$ mice. Colitis was evaluated clinically, histologically and endoscopically. Changes in the mRNA expression of cytokines and antioxidants enzymes were evaluated by RT-qPCR.
**Results:** $Prdx6^{-/-}$ mice exposed to acute and chronic DSS showed a significant decrease in the clinical parameters or in the colon levels of pro-inflammatory cytokines compared to WT mice. In DSS-induced acute and chronic colitis, colon levels of antioxidant enzymes were significantly increased in $Prdx6^{-/-}$compared to WT mice. In addition, total GSH level was increased in $Prdx6^{-/-}$ mice exposed to DSS as compared with the WT. However, overexpression of Prdx6 in mice does not influence the acute and the chronic colitis even a trend towards an amelioration of some cytokines expression in the chronic model.
**Conclusion:** Our data show that the antioxidant Prdx6 deficiency does not affect negatively the DSS-induced acute and chronic colitis but is associated with increased antioxidants enzymes suggesting a critical role of Prdx6 and several compensatory mechanisms during acute chronic colitis. Thus, our finding indicates that cells require well balanced of antioxidant gene to limit excessive inflammation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0805 THE ROLE OF DIPEPTIDYL PEPTIDASES IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** Inflammatory bowel disease (IBD) is a chronic, multi-factorial disease that includes complex interactions between host genetics, the intestinal microbiome and lifestyle factors. Dipeptidyl Peptidase (DPP)-IV is a ubiquitously expressed type-II integral membrane glycoprotein that has been implicated in the immuno-pathogenesis of inflammatory disease including IBD.
**Aims & Methods:** This study retrospectively investigated the role of DPP-IV and other related serine proteases in human IBD. The mRNA expression of DPPIV, DPP8, DPP9, DPP2 and fibroblast activation protein (FAP) was determined in colonic biopsies collected from Crohn's Disease (CD), Ulcerative colitis (UC) and healthy patients (n = 8/group) at the Queen Elizabeth Hospital. RNA was isolated from colonic biopsies using the spin-column technique and cDNA was then synthesized using a reverse transcriptase kit. Relative mRNA expression was quantified using SYBR green technologies. Gene expression data was expressed as the average relative-fold change determined by the comparative Ct method. Sera samples were collected from CD (n = 96) and UC (n = 54) patients at Flinders Medical Centre between 2008 & 2015. Plasma samples from healthy adult donor's (n = 11) were collected at the Women's and Children's Hospital. DPP enzyme activity was quantified by colorimetric enzyme activity assay using the substrate H-Ala-Pro-pNA. Enzyme activity is expressed as median units of activity (U)/mg of protein (range).
**Results:** There was a 6-fold decrease in DPPIV gene expression in CD and UC patient biopsies. DPP8 & DPP9 gene expression was down-regulated 2.5 fold in both CD and UC samples. DPP2 gene expression was unchanged in UC patients; however, in CD patients, there was 3-fold decrease. FAP expression was unchanged in CD patients; conversely, FAP was upregulated 3-fold in UC patients. DPP enzyme activity in the sera was unchanged between healthy 0.41U/mg (0.24–1.11), CD 0.46U/mg (0.14–1.73) and UC 0.54U/mg (0.28–1.23) patient groups.
**Conclusion:** The current study indicates that there is differential DPP gene expression in human IBD; however, further studies are needed to decipher how these changes correspond to disease pathogenesis. Although there was no significant differences in enzyme activity between patient groups, the retrospective data that we have analysed does not specify active and inactive disease. The range of enzyme activity within patient groups suggests that DPP enzyme activity may correspond to disease parameters. We are currently undertaking a prospective study in adult IBD patients to delineate the mechanism of DPPs in the pathogenesis IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0806 ROLE OF EXTRINSIC PRIMARY AFFERENTS AND ASIC 3 IN PELVIC CROSS-ORGAN SENSITIZATION

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**Introduction:** Irritable bowel syndrome and bladder pain syndrome are both characterized by pain in response to organ distension. Epidemiologic studies showed that these two syndromes are often overlapped. Since these pelvic organs share a common extrinsic innervation, it is likely that those syndromes involve a cross-sensitization of the bladder and the colon in response to mechanical distension of the gut.
**Aims & Methods:** The aim of this project was to develop and characterized a rodent model of bladder-colon sensitization. Double retro-labelling was performed to indentify extrinsic primary afferent neurons innervating both the colon (Fluororuby) and the bladder (Flurogold) in the S1–L6 dorsal root ganglia of Sprague Dawley rats. The phenotype of the colon/bladder co-innervating primary afferents was assessed using immunochemistry directed against TRPV4 and ASIC 3. Cross-organ sensitization was obtained in Sprague Dawley rats using echography-guided intravesical administration of acetic acid (0.75%) under brief isoflurane anesthesia. Colonic sensitivity was assessed in conscious rats by measuring abdominal contraction during isobaric colo-rectal distension.
**Results:** Immunohistochemistry showed that 73.1% of extrinsic primary afferents co-innervating the colon and the bladder expressed ASIC 3, and 53.8% expressed TRPV4. By contrast, extrinsic primary afferents innervating the colon or the bladder were positive for ASIC 3 in 39.3 and 42.6%, and for TRPV4 in 70.5 and 57.8% of the case, respectively. Based on these results, colonic hypersensitivity to colorectal distension was observed after intravesical administration of acetic acid (0.75%). This effect started 1 h post-injection and lasted up to 24 h, and was not longer seen after 3 days after injection. Colonic sensitization by intravesical acetic acid administration was prevented by S1 intrathecal administration of APETx2 (2.2$\mu$M), an ASIC 3 blocker.
**Conclusion:** We developed an acute pelvic cross-organ sensitization model in conscious rat. In this model, cross-organ sensitization is likely to involve S1–L6 extrinsic primary afferents co-innervating the colon and the bladder through an ASIC 3 pathway.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0807 INDIAN MIGRANTS HAVE A HIGHER INCIDENCE OF ULCERATIVE COLITIS, MORE SEVERE DISEASE PHENOTYPE AND YOUNGER AGE OF PRESENTATION IN SECOND GENERATION MIGRANTS COMPARED WITH CAUCASIANS: RESULTS FROM A 1-YEAR PROSPECTIVE POPULATION-BASED INCEPTION COHORT STUDY

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**Introduction:** The world-wide incidence of inflammatory bowel disease (IBD) is increasing. Migration influences disease epidemiology. South Asians are the predominant migrant group in the UK with a previously reported highest ulcerative colitis (UC) incidence of 17.2/100.00) and a pan-colonic phenotype.[1] These studies were retrospective and last performed over 10 years ago.[2]
**Aims & Methods:** We aimed to compare the incidence of IBD and disease phenotype of UC at diagnosis between Indians and Caucasians within our catchment area of approximately 500,000 people. All new diagnoses of IBD between February 1st 2015–January 31st 2016 were recorded. Demographic data, ethnicity, smoking status, faecal calprotectin and Simple Clinical Colitis Activity Index (SCCAI) were completed at diagnosis. Data was collated on the validated Epicom database. Information on population size and ethnicity was obtained from 2011 Census data.

**Results:** Eighty-eight patients fulfilled Copenhagen diagnostic criteria for IBD. Eleven living outside the catchment area were excluded. 48/77 were male (Table 1). The predominant ethnic group was Indian (33 cases) with a median age at presentation of 36 years (IQR 29–51) compared with 23 Caucasian cases at 40 years (IQR 33–61.5). The crude incidence of IBD, UC and Crohn's in the Indian group was 26.4, 19.4 and 6.6/100,000 cases respectively compared with 10.7, 7.1 and 2.8/100,000 cases inthe Caucasian group. Average time between symptom onset and diagnosis was 97 days (65–129, 95%CI) for Indians and 56 days (31–81, 95% CI) for Caucasians ($p < 0.001$). Further analysis compared UC between Indians and Caucasians: 50% and 47% had extensive colitis at diagnosis, 81% and 41% never smoked. The median age at diagnosis of first generation Indians was 49 years (IQR 36–65) and was lower in the 2nd generation Indian group compared to Caucasians. (26 years, IQR 20–34 vs 40 years, IQR 33–63, $p < 0.0001$). Indian patients had higher mean SCCAI scores (6.8 vs 4.3), higher mean calprotectin at diagnosis (907 vs 708 ug/g) and lower mean vitamin D levels at diagnosis (16.6 vs 29.8 ng/mL). They also required steroids within 3 months in 8/33 cases vs 2/23 ($p = 0.17$) in Caucasians.

**Table 1:** Demographic and Clinical data comparing Indian and Caucasian groups

| | Caucasian | Indian | Other |
|---|---|---|---|
| **M/F** | 13/10 | 19/14 | 17/5 |
| **Median age at presentation (years)** | 40 (33–62) | 36 (29–51) | |
| **Crude Incidence (cases/100,000)** | | | |
| **IBD** | 10.7 | 26.4 | |
| **UC** | 7.0 | 19.4 | |
| **CD** | 2.8 | 6.6 | |
| **Time to diagnosis (days, 95% CI)** | 56 (31–81) | 97 (65–129) | |
| **Disease phenotype** | | | |
| **E1** | 5 | 9 | |
| **E2** | 4 | 3 | |
| **E3** | 8 | 12 | |
| **1st vs 2nd generation** | - | 19/13 | |
| **Median Age at diagnosis 1st/2nd generation (years)** | - | 41/26 | |
| **Vitamin D (ng/mL, 95% CI)** | 29.8 (14.7–44.5) | 16.6 (9.9–23.2) | |
| **SCCAI at diagnosis (95% CI)** | 4.3 (2.4–6.2) | 6.8 (5.5–6.8) | |
| **Smoking** | | | |
| **Never** | 7 | 18 | |
| **Former** | 8 | 0 | |
| **Current** | 2 | 4 | |
| **Calprotectin before treatment (ug/g, 95% CI)** | 708 (367–1049) | 907 (638–1176) | |
| **Treatment** | | | |
| **Steroids within 3 months** | 2 | 8 | |
| **5-ASA** | 7 | 5 | |
| **Hospital admission** | 3 | 5 | |

**Conclusion:** We report the highest incidence of UC in the Indian migrant population in the literature. The higher SCCAI and calprotectin indicate a more aggressive disease phenotype however the significant delay in diagnosis maybe a confounding factor. Second-generation migrants presented at a younger age than first generation migrants and Caucasians. Migrants have a potential genetic predisposition enhancing susceptibility to environmental exposure. Further studies in first and second-generation migrants examining the impact of factors such as diet on the microbial and metagenomic profille may help to explain the more aggressive disease phenotype and decipher the role of genetics and environment within this group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0808 NATURAL HISTORY OF PERIANAL CROHN'S AND PREDICTORS: LONG-TERM FOLLOW-UP ON A POPULATION-BASED COHORT


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**Introduction:** Perianal Crohn's disease (PCD) is a frequent dreaded condition during Crohn's disease that predicts a disabling course and drastically alters quality of life of patients. Natural history of PCD remains poorly describes, mainly based on retrospective studies from referral centers. The Aims of the present study were to assess the incidence, outcomes and predictors of onset of PCD.
**Aims & Methods:** All incident cases of patients diagnosed with possible CD ($n = 370$) were registered from 1994 to 1997 in Brittany, a limited area in France. At diagnosis were recorded clinical features, endoscopic lesion per ileocolic segment (according to the CDEIS), radiologic and histologic data. All charts of patients were reviewed from the diagnosis to the last clinic in 2015. Cumulative incidence of PCD and each elementary PCD lesions were estimated using the Kaplan-Meier method. Independent predictors of all outcomes were identified using a Cox proportional hazards model.
**Results:** Among the 370 incident cases, 39 had not Crohn's disease and 272 of the 331 cases with CD (82%) were reviewed with a median follow-up of 12.8 years. During the follow-up period, 87 (32%) of patients developed PCD. Cumulative probabilities of PCD occurrence were 22%, 29%, 32% and 24% at 1 year, 5 years, and 10 years and 15 years, respectively. Rectal involvement at diagnosis was independently associated with an increased risk of PCD occurrence ($HR = 1.72$, $p = 0.01$) Cumulative probabilities of perianal ulceration were 14%, 17%, 19% and 21% at 1 year, 5 years, 10 years and 15 years, respectively. No predictor of anal ulceration onset was observed. Conversely ileal disease at diagnosis was associated with less occurrence of anal ulceration ($HR = 0.53$, IC95 [0.29–0.99]). Cumulative probabilities of fistulizing perianal Crohn's disease were 11%, 16%, 19% and 20% at 1 year, 5 years, and 10 years and 15 years, respectively. Perianal ulceration prior to anal fistula ($HR = 13.7$, IC95 [7.33–24.8]) and rectal superficial and/or deep ulceration at diagnosis ($HR = 2.1$, IC95 [1.2–3.65]) were predictors of fistulizing perianal disease occurence. Anal stenosis was never observed without prior history of perianal lesion. Anal stenosis was describe in 13 patients (4%) concomitant to anal ulceration or following fistulizing perianal disease.
**Conclusion:** PCD are frequently observed during Crohn's disease for broadly one third of patient. These data underline the need to early treat patient with rectal involvement and anal ulceration to avoid the onset of fistulizing perianal disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0809 CLOSTRIDIUM DIFFICILE INFECTION WORSEN OUTCOME OF HOSPITALIZED PATIENTS WITH INFLAMMATORY BOWEL DISEASE


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**Introduction:** The prevalence of *Clostridium difficile* infection (CDI) in inflammatory bowel disease (IBD) patients has been reported increasing rapidly over the past several decades in North America and Europe. However, the exact global epidemiology is hindered due to lack of data from developing countries.
**Aims & Methods:** In the present study, we sought to evaluate the prevalence and risk factors of CDI and the impact of CDI on IBD patients. A total of 646 hospitalized adult IBD patients were enrolled; and their fresh stool specimens were acquired and used for *Clostridium difficile* detection. Clinical data were collected to evaluate IBD disease progression with two years following-up. Potential risk factors including demography, IBD disease characteristics within one year and pre- and in-hospital concomitant medication use within six months were recorded.
**Results:** The incidence of CDI in CD patients (12.7%) was significantly lower than that in UC patients (19.3%); and the most common toxin type was $A^+B^+$ strains. Length of stay, hospitalization times and bowel surgery rate were significantly higher in CDI than non-CDI group either in CD or in UC patients. Moreover, more patients in CDI-CD group were still in active and even clinical moderate or severe CD stage than non-CDI-CD group after two years following-up. Fistula, antibiotics and infliximab usage were likely to increase the CDI rate in CD patients, while risk factor in UC patients was infliximab treatment.
**Conclusion:** CDI is a growing public health issue and may influence the IBD course, increase the expenditure even delay remission of IBD patients. Increasing attention need to be paid to complication of IBD by CDI urgently.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0810 INFLAMMATORY BOWEL DISEASE AND COLORECTAL CANCER: INTERIM ANALYSIS OF A SINGLE CENTER RETROSPECTIVE CHART REVIEW


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**Introduction:** Colorectal cancer (CRC) is perhaps the most undesirable adverse outcome in inflammatory bowel disease (IBD).

**Aims & Methods:** The aim of this study is to estimate the rate of CRC in a single center cohort of IBD patients and to identify potential predisposing factors. A retrospective review of the endoscopy charts of the period 1996–2016 was conducted. All patients enrolled exhibited both endoscopic and histologic documentation of IBD. Patient and disease (Montreal classification) characteristics, change in location and behaviour of IBD, location of CRC and treatment with imunomodulators and antiTNFalpha agents were recorded. As index colonoscopy was defined the one that established IBD diagnosis.

**Results:** So far, 550 IBD patients having undergone 1805 colonoscopies have been registered. Males are 279 [50.7%]. Median age at IBD diagnosis is 41 years [IQR: 27–55, range: 2–89]. Median follow-up period is 37.2 months [IQR: 3.5–94.6, range: 0–504.4]. Ulcerative colitis (UC) was diagnosed in 274 [49.8%], Crohn's disease (CD) in 272 [49.5%] and IBD unclassified in 4 [0.7%] patients. IBD location changed in 49 UC [17.9%] and in 32 CD [11.7%] patients. CD behaviour progressed to a worse state in 21 [7.7%] patients. Eight patients [1.5%] developed CRC; 2 with CD ileocolitis (both in the right colon) and 6 with UC of who 4 were classified as having extensive colitis (two rectal, one in the right and one in the left colon) and 2 as having left-sided colitis (both in the left colon). None of these patients had been operated for IBD. A non-passable colonic stenosis was already known before CRC diagnosis in only one patient while no apparent stenosis had been detected in the rest. Two patients with CRC received azathioprine for more than 3 years, whereas none was treated with an anti-TNFalpha agent.

**Conclusion:** The rate of CRC is low in our cohort of IBD patients and compatible with literature data regarding Caucasian populations. No association was observed with specific predisposing factors that were studied.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0812 IMPACT OF BIOLOGICAL THERAPY ON IBD HOSPITALIZATIONS OUTCOMES: REPORT FROM AN ITALIAN TERTIARY CENTRE BETWEEN 2000 AND 2013


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**Introduction:** In recent years the management of Inflammatory bowel disease (IBD) is changing, in particular, due to the introduction of biological therapy. New advances in this context made progressively possible to manage these conditions in the outpatient setting. While the advantages of biological therapy are unquestionable, there is still controversy if they can truly modify disease outcomes.

**Aims & Methods:** Aim of the study was to describe IBD admissions and outcomes variations between the pre- and post- biologic era in an Italian tertiary centre between the years 2000 and 2013. All hospitalizations for Crohn's disease (CD) or ulcerative colitis (UC) were indentified from Policlinico "A. Gemelli" between 2000 and 2013 using ICD-9-CM codes for IBD. Hospitalization outcomes were stratified in 3 groups (elective restaging, therapy administration or unrelated). Surgery and complications related to IBD during the hospitalization were also evaluated. For CD the year 2003 was used as "cut-off" for pre- and post- biologic era, while 2007 was used for UC, as those were the years of introduction of biologics at Policlinico "A. Gemelli". Statistical analysis was performed by Chi2 test for qualitative variables and the Student's t test for quantitative variables. Statistical significance was defined for p values less than 0.05.

**Results:** Between the years 2000 and 2013 an overall of 8834 admissions were recorded at "Policlinico A. Gemelli" for IBD, specifically, 52.3% CD and 47.7% UC. Hospitalizations due to IBD increased reaching a peak in 2006, with a downward trend in the following years. Analyzing hospitalization outcomes we found a statistically significant difference between pre- and post- biologic groups for both CD and UC, with a relative increase in the therapy administration group. A surgical procedure was required in 10.8% of admissions, in particular 11.0% for CD and 10.7% for UC, without difference between pre- and post-biologic era in both the diseases. Complications occurred in 28.7% of admissions, 31.6% for CD and 25.5% for UC. The most common complications were fistula (10.1%) for CD and osteo-articular manifestations for UC (6.6%). We did not find differences in the overall occurrence of complications between pre- and post-biologic era in both the diseases, however we noted a variation in the incidence of single complications.

**Conclusion:** Hospitalizations due to IBD are now decreasing, consistently with the hypothesis that introduction of biologic therapy is associated with a progressive switch to the outpatient management. However, initial necessity of hospitalization for patients receiving biologics may explain the relative raise in admissions for therapy administration in the post-biologic era. About 11% of admitted patients underwent a surgical procedure related to IBD. We did not find difference in surgical procedure occurrence after biologic introduction for both diseases. About 23% of admitted patients presented an IBD-related complications, which were also slightly more frequent in CD. Introduction of biologics is associated with variation in the incidence of IBD-related complications.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0813 PREVALENCE OF IRON DEFICIENCY WITHOUT ANAEMIA IN INFLAMMATORY BOWEL DISEASE AND ITS IMPACT ON THE QUALITY OF LIFE


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**Introduction:** Iron deficiency without anaemia (IDWA) is a common finding in patients with inflammatory bowel disease (IBD). The real magnitude of this issue and its consequences are unknown, although it is underestimated.

**Aims & Methods:** To determine the prevalence of IDWA, identifying factors related to this condition and its impact on quality of life of patients. We evaluate the medical approach of this situation. We carried out an observational, transversal and single-centre study from population-based Córdoba IBD cohort. Consecutive patients were included from April to June 2015, and demographics, clinical and laboratory data were collected. IDWA was defined as ferritin levels $< 30$ or $< 100$ ng / mL with absence or presence of inflammatory activity respectively, with normal levels of hemoglobin. Univariate and multivariate analysis was performed to identify predictor factors, comparing IDWA patients with those without iron deficiency. The quality of life was assessed with the IBDQ-9 and FACIT-F questionnaires. The medical management was assessed.

**Results:** 127 patients (58.3% men and 41.7% women, mean age $42.27 \pm 12.08$ years) diagnose with IBD were included. The prevalence of IDWA was of 37%, normal iron deposits with normal levels of hemoglobin was 50.4% and 12.6% anaemia. In multivariate analysis the female gender (OR = 2.8, 95% CI: 1.2–6.6, $p = 0.015$) and inflammatory activity (OR = 9.4, 95% CI: 2.5–35.9, $p = 0.001$) were the variables associated with IDWA. Excluding the patients with anaemia, the group with IDWA had a worse quality of life (with a lower score in IBDQ-9 and FACIT-F questionnaires which decreased 6.55 and 4.26 points, respectively, compared to the group with normal deposits). Extreme fatigue was higher in the IDWA group, 64.7% versus 35.3%. In less than 30% of cases, an active therapeutic approach (like oral iron supplements) was performed.

**Conclusion:** Over one third of patients with IBD showed IDWA. Factors as the female gender and the inflammatory activity of the disease were associated with a higher prevalence of this complication. The IDWA had a negative impact on the quality of life of patients. An active and optimized therapeutic approach is required.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0814 DEVELOPMENT AND VALIDATION OF A TANDEM LIQUID CHROMATOGRAPHIC MASS SPECTROMETRIC (LC-MS/MS) ASSAY FOR THE MEASUREMENT OF VEDOLIZUMAB (VLZ) LEVELS IN PATIENT SERUM

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**Introduction:** Vedolizumab (VLZ), an $\alpha4\beta7$ integrin antagonist, is a therapeutic monoclonal antibody recently approved for use in moderate to severe ulcerative colitis and Crohn's disease. As for TNFa agonists, measurement of serum levels is indispensable for the optimization of VLZ therapy. Typically, ligand binding assays (LBA), such as enzyme-linked immunosorbent assays (ELISAs), are used to measure serum antibody levels. However, LBAs may have significant limitations, including procurement or generation of the binding reagents, interference from matrix components, and drug antibodies. To overcome these limitations, we have developed a reliable tandem liquid chromatographic mass spectrometric (LC-MS/MS) method to quantify VLZ serum levels.

**Aims & Methods:** Serum analyses were performed on an ultra performance liquid chromatography (UPLC)-MS/MS system (Ultimate 3000 Binary RSLC system, Thermo Scientific, Waltham, MA, USA) coupled to a TSQ Vantage triple quadrupole mass spectrometer (Thermo Scientific, Waltham, MA, USA) with an H-ESI II ionization source. The analytical column was an Acquity UPLC BEH Shield RP C18 2.1 mm × 50 mm column with 1.7$\mu$m particle size. The mobile phases were KM9600LMA and KM96LMB. VLZ was extracted from serum by a modified ''pellet digestion'' technique. Tryptic peptides for quantification were identified for VLZ using a selective reaction monitoring (SRM) mass spectrometry method.

**Results:** Sensitivity for VLZ was determined to be 1.6$\mu$g/mL. The standard curves showed high reproducibility and sensitivity. Intra- and inter-assay precision were 10.46% and 7.67%, respectively, and accuracy was within 20%. There was no significant interference from lipemic, hemolyzed, or rheumatoid factor (Rf) serum.

**Conclusion:** A general LC-MS/MS method approach using immunocapture was developed, qualified, and applied to VLZ quantification in serum, with an affinity purification time of one hour. The method has been demonstrated to be accurate, precise and robust. The LC-MS/MS method may also be applied to other protein-based drugs to accurately detect serum drug levels.

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J. Stein: Jürgen Stein has received fees for lectures and consultancy from Immundiagnostik AG, Bensheim, Germany
All other authors have declared no conflicts of interest.

## P0815 THE INFLUENCE OF VITAMIND ON EXPRESSION OF CYTOKINES MRNA IN IBD

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**Introduction:** The aetiology of Crohn's disease (CD) and ulcerative colitis (UC) is not known. Recent data suggest that vitamin D (VD) plays an important role in IBD. Pathways that are influenced by VD in IBD are poorly understood.

**Aims & Methods:** The aim of this study was to analyse the influence of 25(OH) VD serum concentration on the expression of mRNA proinflammatory cytokines (IL-6,IL-23, TNF$\alpha$, CCR1), regulatory cytokines (IL-10,TLR2,CCR9, CD 207) and transcription factor Fox3P in colonic mucosal samples from IBD patients. We performed a cross-sectional study. The cohort consisted of 87 IBD patients (47 CD and 40 UC) followed at the IBD centre of University Hospital Bratislava-Ružinov. We performed colonoscopy in each patient and took biopsies from inflammed and if applicable also from non-inflammed mucosa from sigma (CD, UC) and terminal ileum (CD). Serum concentration of 25(OH) VD was assessed in each patient at the time of colonoscopy. mRNA was extracted from mucosal biopsy samples for each cytokine and isolated by RLT buffer. mRNA was reversely transcribed. We normalized expression of the target genes to the expression of the house-keeping gene (GAPDH). Then we analysed the correlation between serum concentration 25(OH) VD and the expression of mRNA of inflammatory cytokines from biopsies samples.

**Results:** In CD we observed a positive correlation of serum concentration of 25(OH) VD and mRNA expressions levels of TNF$\alpha$ ($r = 0.41$, $p = 0.043$), IL-6($r = 0.45$, $p = 0.023$), IL-10($r = 0.44$, $p = 0.027$), IL-23($r = 0.55$, $p = 0.023$), TLR 2($r = 0.041$, $p = 0.042$) in inflammed mucosa of terminal ileum. A positive correlation was also observed with CCR5($r = 0.042$, $p = 0.011$) and CCR1($r = 0.33$, $p = 0.027$) in non-inflammed mucosa from sigma. We also found a positive correlation between 25(OH) VD and IL-23($r = 0.45$, $p = 0.011$), TLR4($r = 0.42$, $p = 0.017$), CD 207($r = 0.42$, $p = 0.017$), CCR1 ($r = 0.52$, $p = 0.002$), CCR5 ($r = 0.51$ $p = 0.003$) and CD 206($r = 0.43$, $p = 0.014$) in non-inflammed mucosa of sigma in UC.

**Conclusion:** According to our results, VD significantly influences the levels of expression of several inflammatory cytokines including TNF$\alpha$ in colonic mucosa of patients with CD as well UC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0816 DEVELOPMENT OF A DIAGNOSTIC SCORING SYSTEM TO PREDICT MICROSCOPIC COLITIS

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**Introduction:** Many patients presenting with diarrhoea undergo colonoscopy with random biopsies to rule out microscopic colitis (MC), if the colonoscopy is macroscopically normal. However, the yield of taking biopsies in individuals with diarrhoea is low (1). Accurate predictors of MC could identify at-risk individuals, and avoid the need to take biopsies in a substantial proportion of patients, saving money for the health service. We previously derived and validated a diagnostic scoring system for MC based on clinical information alone but this was based on retrospective data (2).

**Aims & Methods:** The aim of this study was to validate the original scoring system in a prospective cohort of patients, and to assess whether incorporating further clinical features could improve its performance. Consecutive adults with loose stools undergoing colonoscopy in Leeds, UK were included. Demographic and symptom data were collected prospectively. Patients with a diagnosis of microscopic colitis including both collagenous and lymphocytic colitis, after histological examination of biopsy specimens, were compared with those with normal biopsies. The diagnostic scoring system described previously, which assigned scores for female gender, current use of proton pump inhibitors or non-steroidal anti-inflammatory drugs, age $\geq$ 50 years, weight loss and the absence of abdominal pain, was applied. In addition, the incorporation of other factors, including other drugs that may be associated with MC (statins and selective serotonin re-uptake inhibitors), number of stools, nocturnal passage of stools, and duration of loose stools, into the scoring system was assessed. Sensitivities, specificities, and positive and negative predictive values were calculated for the modified scoring system.

**Results:** In total, 242 patients (mean age 51.0 years, 163 (67.4%) female), 26 (10.7%) of whom had MC, were included. A cut off of $\geq$4 on the original scoring system had a sensitivity of 92.3% and specificity of 35.2% to detect MC. After including the additional clinical factors, nocturnal passage of stools and duration of loose stools $<$6 months were both found to be significant predictors of MC. Incorporating these variables into a modified scoring system using a cut off of $\geq$6 identified MC with 95.7% sensitivity and 46.0% specificity.

**Conclusion:** Incorporating nocturnal passage of stools and duration of loose stools into our original scoring system may improve ability to predict MC, and avoid random colonic biopsies in a greater proportion of patients with loose stools. Future studies in clinical practice could use this scoring system, alongside biochemical or faecal markers, in the diagnostic pathway for MC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0817 THE ROLE OF FAECAL CALPROTECTIN IN A PRIMARY CARE REFERRAL PATHWAY IN THE UK

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**Introduction:** Faecal calprotectin (FCP) is a clinically useful surrogate marker of intestinal inflammation in Inflammatory Bowel Disease (IBD). Multiple studies confirmed its high negative predictive value (NPV) and low positive predictive value (PPV) for a diagnosis of IBD. This indicates a possible clinical utility in primary care settings to avoid unnecessary referrals to secondary care.
**Aims & Methods:** To evaluate the clinical impact of FCP in a population-based setting in a diagnostic referral pathway for primary care practitioners. Methods. we investigated the outcome of all FCP tests performed in primary care from 1st of May 2015 till 31 of August 2015 in a population-based setting including 703.983 individuals residing in the city of Nottingham, East Midlands. Descriptive statistics were used to summarize the patient demographics and referrals to secondary care. We analysed the impact of GP interpretation of FCP in the context of the clinical presentation and reviewed all electronic records of referrals to secondary care. We used area under the receiver operating characteristic (AUROC) curve for this group to obtain negative and positive predictive values with an FCP cut off of 50 ug/g. The test was considered positive for detection of IBD if the outcome was diagnosis of ulcerative colitis (UC) or Crohn's disease (CD).
**Results:** The total number of tests performed was 809 on 731 patients with no previous history of IBD. There was a female predominance with a ratio of 1.7. The median age was 40 years(IQR = 26). FCP levels were low (< 50ug/g), medium (50–200ug/g) or high (> 200ug/g) in 398, 202 and 131 patients respectively. 23.9%, 42.6% and 71.8% of the patients who had low, medium and high FCP in primary care respectively were referred to secondary care. The total number of referrals was 275 patients. A similar female predominance (ratio = 1.6) and age group (median = 40, IQR = 29) was maintained in the referred cohort. IBD was then confirmed in 10 patients with CD and 5 patients with UC. Twelve patients had high, three had medium and none had a low FCP on presentation to primary care. In the cohort referred to secondary care, FCP had a NPV and PPV of 100% and 8% respectively with a specificity of 37% and a sensitivity of 100%. Ninety-five patients referred with negative FCP had further investigations at the discretion of the hospital clinician: 58 colonoscopies, 19 gastroscopies and 3 MRI small bowel. None of which was diagnosed with IBD.
**Conclusion:** FCP maintains its high NPV and low PPV in real life primary care practice. Of the patients referred to secondary care with a negative FC none had an eventual diagnosis of IBD. A considerable proportion of patients with a negative FCP at presentation were still investigated in secondary care. Our data indicates that FCP may be a reliably good negative test to be used in a primary care referral pathway. Further education of its use is needed for both primary and secondary clinicians to avoid unnecessary referrals and invasive investigations in low risk subgroups
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0818 COLONOSCOPY SURVEILLANCE IN LONG-STANDING INFLAMMATORY BOWEL DISEASE IN A GENERAL DISTRICT HOSPITAL AND COMPARISON BETWEEN WHITE LIGHT ENDOSCOPY AND CHROMOENDOSCOPY IN DETECTING DYSPLASIA DURING SURVEILLANCE

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**Introduction:** The increased risk of colorectal cancer in the Inflammatory Bowel Disease (IBD) population along with the global IBD incidence rise highlights the importance of colonoscopy surveillance programme. Recent guidelines advocate use of chromoendoscopy as a preferable mode used for surveillance.
**Aims & Methods:** The aim of our study was to assess adherence of our IBD population with disease > 10 years to colonoscopy surveillance and also compare chromoendoscopy with white light endoscopy against their ability to detect dysplasia. Data from our trust IBD registry were analysed retrospectively. From a total IBD population of 2254 patients, 820 were identified as having IBD for 10 years or more and were included. Two groups, one receiving chromoendoscopy and one white light endoscopy for surveillance performed in real-life practice, were compared. Data were analysed according to number of patients having a dysplastic lesion in endoscopy with Z-score test. Type of lesion and grade of dysplasia were also taken into account.
**Results:** Out of 820 patients, 610 were suitable for surveillance; n = 449 with Ulcerative colitis (UC)/indeterminate colitis (IC) and n = 161 with Crohn's colitis (CD). Colonoscopy surveillance was initiated in n = 216 (48.1%) of the UC/IC group and n = 105 (65.2%) of CD patients. Surveillance was not continued as per guideline (with maximum interval of 5 years) in n = 37 patients (29.8%) of UC/IC and n = 13 (22.4%) of CD patients. Average time of initiating surveillance was 13 years. Only 18% of surveillance colonoscopies performed using chromoendoscopy. Chromoendoscopy (CE) was performed in 59 patients during 2012–2015. 38 were male with mean age 59 (SD 13.6). A similar group of 59 patients were white light endoscopy (WLE) was performed was randomly selected from our initial sample. A total of 16 dysplastic lesions (2 with high grade dysplasia (HGD) and 14 with low grade dysplasia (LGD)) were detected in 12 patients in the CE group and 12 lesions (1 HGD and 11 LGD) were detected in 9 patients in the WLE group but results didn't reach statistical significance(p = 0.47). In the CE group 7 lesions were due to flat dysplasia (43.75%) compared to only 1 flat lesions in the WLE group (8.3%) (p = 0.02).
**Conclusion:** Adherence to guidelines for colonoscopy surveillance was poor both for UC/IC and CD population. Similarly low rates (44%-54%) were observed in studies of other European countries like the Netherlands, Ireland and France. Reasons for poor uptake of surveillance need to be identified. The number of dysplastic lesions found was greater with CE. In addition CE was found to be superior to WLE in identifying flat dysplastic lesions in IBD surveillance population. This reflects results from recent meta-analysis included in the SCENIC international consensus on surveillance in IBD but larger randomized trials are still required.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0819 ENDOSCOPY SIGNIFICANTLY IMPROVES OUTCOME PREDICTION IN ACUTE SEVERE COLITIS

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**Introduction:** Up to one-third of patients with acute severe colitis will present an insufficient response to systemic steroids and will require rescue therapy or surgery. Delay in surgery has been associated with increased postoperative complications. Early recognition of patients who will show an insufficient response is therefore of the utmost importance.
**Aims & Methods:** To compare several endoscopic index in the setting of acute severe Ulcerative Colitis. We evaluated consecutive patients admitted with acute severe colitis according to the Truelove & Witts criteria. For each patient the Mayo endoscopic subscore, the Ulcerative Colitis Endoscopic Index of severity (UCEIS) and the Ulcerative Colitis Colonoscopic Index of Severity (UCCIS) were determined. Outcomes included the need for medical rescue therapy, steroid refractoriness and surgery.
**Results:** We included 76 patients, median age 34.5 years (15–80) with median Truelove & Witts score of 4 (2–5). 20 patients (26.3%) required rescue therapy (16 with Infliximab and 4 with Cyclosporine), 26 patients (34.2%) were colectomized and 3 patients (3.9%) died. Median endoscopic scores were: Mayo 3 (1–3), UCEIS 5 (2–7) and UCCIS 45.8 (13.8–59.8). Only UCEIS and UCCIS were predictors of surgery (AUC 0.723, p = 0.002 and AUC 0.733, p = 0.001) but only the UCCIS adequately predicted unresponsiveness to steroids (AUC 0.675, p = 0.009). A compound outcome including steroid refractoriness, surgery and death was also only predicted by UCCIS (AUC 0.644, p = 0.045). In a logistic regression model including age, gender, disease extension, Truelove and Witts score, C-reactive protein and endoscopy, the UCEIS (OR 2.47 CI95% [1.18–5.16], p = 0.016) and the UCCIS (OR 1.12 CI95% [1.023–1.23] but not the Mayo were predictors of the need for surgery.
**Conclusion:** In this retrospective study, endoscopic severity was an excellent predictor of important outcomes in acute severe colitis. The UCCIS appear to perform better than the UCEIS in all outcomes. The complexity of the former can represent the greatest barrier to its implementation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0820 RISK OF COLORECTAL ADENOMAS IN PATIENTS WITH MICROSCOPIC COLITIS: A CASE-CONTROL STUDY

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**Introduction:** Previous case-control studies have shown a low rate of colorectal polyps in patients with microscopic colitis (MC), but the control groups used were heterogeneous (1–3).
**Aims & Methods:** The aim of the study was to evaluate this association in comparison with a control group with chronic diarrhoea and a control group of individuals of average risk.
One hundred patients with MC (Group A) (age, 62.1 ± 1.5; 68% women; 44 aged between 50–70 years) and 200 patients with chronic diarrhoea and normal colon histology (Group B), matched for age and sex were included. Diagnostic colonoscopy including multiple colonic biopsies was performed in the same period of time. Reports of colonoscopy and histology of both index colonoscopy and previous colonoscopies were reviewed. Colorectal polyps (number and size) and their histology were recorded. A control group from a population screening program for colorectal cancer by colonoscopy (COLONPREV study) matched for age and sex (Group C), was randomly selected (n = 88; age 50 to 70 years). A conditional logistic regression (1 case with 2 controls) was performed.
**Results:** 15% of patients in Group A and 18.5% in Group B had adenomas (OR = 0.76; 95% CI = 0.4–1.5; p = 0.43). In the 50 to 70 years age group, the presence of adenomas was: Group A, 13.9%, Group B, 18.2% and Group C, 29.5%. The OR of the analysis of Group A vs Group C was 0.33 (95% CI = 0.12–0.93; p = 0.036), and Group B vs Group C was 0.45 (95%CI = 0.20–0.98; p = 0.047). The frequency of advanced adenomas was: Group A 4% (OR = 0.26, 95%CI = 0.08–0.85 vs Group C), group B 5% (OR = 0.33; 95%CI = 0.1–0.8 vs Group C), and Group C 13.6% (1 patient with colorectal cancer).
**Conclusion:** Patients with MC have a low rate of colorectal adenomas and lesser histological severity as compared to the average risk population. However, the absence of differences with the group of chronic diarrhoea and normal colonic histology suggests more an effect of chronic diarrhoea than of colonic inflammation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0821 POST-INDUCTION SERUM INFLIXIMAB TROUGH LEVEL WAS ASSOCIATED WITH MUCOSAL HEALING AFTER INITIATING THERAPY IN CROHN'S DISEASE

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**Introduction:** Serum infliximab trough level(S-IFX) and antibody were documented to correlate with clinical response. Aim of this study was to identify relationship between trough levels, antibodies and mucosal healing (MH) in a cohort on maintenance infliximab therapy.
**Aims & Methods:** 108 patients were retrospectively enrolled. All received a scheduled maintenance therapy after response to infliximab induction. S-IFX and antibodies were tested in at 14 weeks after initiating treatment. Endoscopic activities were evaluated at 14 and 52 weeks.
**Results:** At week 14, S-IFX was 4.78 ± 6.16ug/ml and 19% (21/108) of patients developed antibodies. S-IFX was significantly lower in patients with antibody (1.49 ± 3.05ug/ml vs 5.58 ± 6.46ug/ml, P < 0.01). 52 of 102 patients reached MH. S-IFX were higher in patients with MH (6.26 ± 7.78ug/ml vs 3.32 ± 3.80ug/ml, P = 0.02). But there was no statistical difference on MH between ATI positive and negative groups (36% vs 54%, P = 0.17). During 52 weeks follow up, 28% (30/108) patients lost of response to infliximab. The patients who lost of response had lower S-IFX and higher ATI positive rate than patients had sustained response (2.16 ± 3.05ug/ml vs 6.50 ± 8.02ug/ml, P = 0.03; 48% vs 23%, X = 5.11,P = 0.02). At week 52, 73 patients had undergone endoscopy and 31 patients reached MH. Patients with MH had relatively higher S-IFX than who did not reach MH (7.77 ± 9.13ug/ml vs 2.99 ± 3.23ug/ml, P < 0.01), but no statistical difference for antibodies between two groups (31% vs 45%,P = 0.30). S-IFX had a predictive value on MH in 52 weeks follow up. When S-IFX > 2.5ug/ml, the sensitivity for predicting MH at 52 wks were 87%, and the specificity were 61%(AUC = 0.73,P < 0.01).
**Conclusion:** Post-induction serum IFX trough level could predict MH in CD patients undergoing IFX treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0822 PREDICTORS OF TISSUE HEALING IN ULCERATIVE COLITIS PATIENTS TREATED WITH ANTI-TNFA AGENTS

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**Introduction:** Assessment of tissue healing has become of paramount importance in patients treated for inflammatory bowel disease. The aim of our study was to prospectively identify, at diagnosis, factors predictive of mucosal healing in ulcerative colitis (UC) patients treated with anti-TNFα.
**Aims & Methods:** All consecutive patients with UC who had corticosteroid-refractory or corticosteroid-dependent disease and were eligible for treatment with anti-TNFα agents (infliximab, adalimumab, golimumab), according to the current ECCO guidelines were considered for enrolment in the study. Patients on azathioprine received anti-TNFα treatment, immunomodulatory- and anti-TNFα-naïve patients received combination therapy with azathioprine and anti-TNFα, whereas anti-TNFα monotherapy was offered to patients aged less than 25 and over 65 years and in those who refused combination therapy. Patients on combo who discontinued azathioprine shortly after initiation of treatment for drug-related adverse events were grouped with the anti-TNFα monotherapy treated patients. The duration of azathioprine co-treatment in combo was 6 months. Patients who consented to participate in the study underwent ileocolonoscopy with biopsies of the affected areas and assessment of UC disease activity (total Mayo score calculation) prior to and at 3 and 12 months after initiation of anti-TNFα treatment. Complete mucosal healing (CMH) was strictly defined as endoscopic sub-score 0. In a subgroup of patients the mucosal expression of T helper (Th) cell lineage-specific transcription factors (T-bet, Gata3, Rorc, FoxP3) and the concentration of cytokines in the serum (IL-10, IL-6, IFN-γ, IL-17A) were measured by real-time RT-PCR and ELISA respectively and their predictive value for mucosal healing at 1 year was examined.
**Results:** From September 2010 till January 2015, 67 UC patients treated with infliximab (n = 56), adalimumab (n = 5) or golimumab (n = 6) were enrolled in the study. At the end of 1 year, only 29 (43.3%) patients achieved CMH. Patients receiving anti-TNFa and concomitant azathioprine treatment for the first 6 months showed higher rates of CMH, as compared to those receiving anti-TNF monotherapy and those that discontinued azathioprine during the first month because of side-effects [CMH: 28 patients with combination therapy and 1 in monotherapy; without CMH: 30 patients with combination therapy and 8 in monotherapy; p = 0.03]. In the subgroup of 12 patients in whom immunological markers were sought, responders had significantly lower baseline expression of the transcription factor T-bet that defines type 1 (Th-1) adaptive immunological responses (p < 0.05). Finally, responders had significantly lower baseline serum concentration of IL-6 (p < 0.05).
**Conclusion:** Immunomodulator use, lower baseline mucosal expression of T-bet as well as lower baseline serum concentration of IL-6 are associated with complete mucosal healing in UC patients treated with anti-TNFα.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0823 CLINICAL SIGNIFICANCE OF PERIPHERAL BLOOD TH17 CELLS IN EVALUATING DISEASE ACTIVITY OF INFLAMMATORY BOWEL DISEASE: A MULTI-CENTER CLINICAL STUDY

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**Introduction:** Th17 cells play important roles in immuno-inflammatory responses. The relationship between Th17 cells and inflammatory bowel disease (IBD) is a new hot spot of related studies.
**Aims & Methods:** Aims: To investigate preliminarily the role of Th17 cells in the pathogenesis of IBD and the clinical significance of peripheral blood Th17 cells in evaluating disease activity. Methods: Peripheral blood mononuclear cells were collected in 162 IBD patients recruited from 5 hospitals, including 78 Crohn's disease (CD) and 84 ulcerative colitis (UC), and also 80 healthy volunteers. The proportion of Th17 cells in peripheral blood $CD4^+$ T cells was detected with flow cytometry after stimulated by PMA and ionomycin. Simultaneously, two clinical inflammatory markers, ESR and serum CRP were measured.
**Results:** The proportion of peripheral blood Th17 cells was significantly higher in CD group (2.51%±1.59%) and UC group (4.15%±2.75%) than in control group (1.44%±0.73%, P all <0.05), and that in UC group was significantly higher than in CD group (P < 0.01). Furthermore, the proportion of peripheral blood Th17 cells in IBD patients was significantly higher in active stage than in remission stage (CD: 3.39%±1.56% vs. 1.48%±0.81%, P < 0.01; UC: 5.77%±2.77% vs. 2.18%±0.59%, P < 0.01). In Spearman rank correlation coefficient analysis, the proportion of peripheral blood Th17 cells in active stage CD and UC was correlated significantly with ESR ($r_s = 0.851$, P < 0.05; $r_s = 0.817$, P < 0.05) and CRP ($r_s = 0.793$, P < 0.05; $r_s = 0.873$, P < 0.05).
**Conclusion:** Th17 cells might be involved in the pathogenesis and development of IBD, especially UC. Measurement of the proportion of peripheral blood Th17 cells is beneficial for the evaluation of disease activity of IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0824 A NOVEL FECAL CALPROTECTIN ASSAY USING THE LATEX AGGLUTINATION TURBIDIMETRIC IMMUNOASSAY IS USEFUL FOR ULCERATIVE COLITIS PATIENTS IN EVALUATION OF MUCOSAL HEALING


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**Introduction:** We have reported that a quantitative fecal immunochemical test (FIT) could predict mucosal status of UC as well as or better than fecal calprotectin (Fcal). Additionally, the cost and time benefit of FIT are superior to those of Fcal. However, the usefulness of Fcal has been well-verified for detecting the changes of mucosal inflammation of UC patients in the world. Although it is desirable to weigh the two markers for more precise estimation of mucosal status of UC, there is no any assay which can measure levels of the two markers easily. In recent days, we've invented the break-through assay which could measure levels of the hemoglobin and calprotectin simultaneously by a single sampling probe with latex agglutination turbidimetric immunoassay (LATIA) reagents.
**Aims & Methods:** The aim of this study is to evaluate the usefulness of a novel fecal calprotectin assay (Fcal-LATIA). Consecutive UC patients who underwent scheduled colonoscopy between March 2015 and February 2016 were requested to bring fecal samples with the OC-Auto Sampling Bottle 3 (Eiken Chemical, Japan) for the examination of FIT and Fcal. Levels of FIT and Fcal were analyzed from the same samples. FIT levels were determined with OC-SENSOR DIANA (Eiken Chemical, Japan) according to manufacturer's instruction (using the LATIA reagent). Fcal levels were determined by two methods, conventional enzyme-linked immunosorbent assay (ELISA) and newly developed LATIA reagent. For ELISA, Fcal levels were determined with commercially available ELISA kit (Immundiagnostik, Germany) according to manufacturer's instruction. For LATIA, the levels were determined with OC-SENSOR DIANA using the LATIA reagent. The measuring time of OC-SENSOR DIANA is about 10 minutes per 1sample. The mucosal status of UC patients was assessed via the Mayo endoscopic subscore (MES) classification. Evaluation was performed at each portion of the colorectum (cecum and ascending colon combined, transverse colon, descending colon, sigmoid colon, and rectum).
**Results:** In total, 120 UC patients were evaluated in conjunction with the fecal marker and colonoscopic findings. First, we evaluated the correlations between Fcal-LATIA and Fcal-ELISA, a significant correlation was also observed between the Fcal-LATIA values and Fcal-ELISA values (Spearman rank correlation coefficient: 0.96, $p < 0.0001$). Secondly, the correlation between fecal markers (FIT, Fcal-LATIA, Fcal-ELISA) and colonoscopic findings were analyzed. All of these fecal markers were significantly correlated with the maximum MES (Spearman rank correlation coefficient, FIT: 0.75, $p < 0.0001$, Fcal-LATIA: 0.58, $p < 0.0001$, Fcal-ELISA: 0.60 $p < 0.0001$). When mucosal healing was defined as MES 0 alone, the sensitivity and specificity of FIT was better than those of Fcal by two methods. Whereas the sensitivity and specificity of Fcal by two methods is similar. (The cutoff determined by ROC analysis: $<50$ ng/mL for FIT, $<220$ μg/g for Fcal-LATIA, and $<280$ μg/g for Fcal-ELISA: Sensitivity: 0.90 vs. 0.77 vs. 0.83, Specificity: 0.80 vs. 0.80 vs. 0.75) (The standard cutoffs: $<100$ ng/mL for FIT and $<250$ μg/g for Fcal: Sensitivity: 0.93 vs. 0.77 vs. 0.77, Specificity: 0.80 vs. 0.80 vs. 0.75). Similar AUCs were obtained by ROC analysis for the FIT and two Fcal results (0.86 vs. 0.83 vs. 0.84).
**Conclusion:** A novel Fcal assay using the LATIA reagent is a rapid assay, and correlated significantly with conventional Fcal assay (ELISA). In addition, Fcal-LATIA was effectively predicted mucosal healing in UC patients. A novel assay Fcal-LATIA, simultaneously measured with FIT, could help a fine quality practice for UC patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0825 MEASURING APPARENT DIFFUSION COEFFICIENT VALUES IN COLLAPSED AND DISTENDED SMALL BOWEL LOOPS HAS A POTENTIAL IN EXCLUDING INFLAMMATORY BOWEL DISEASE IN PATIENTS WITHOUT BOWEL PREPARATION: A STUDY IN HEALTHY SUBJECTS


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**Introduction:** Up to 15% of patients suspect for inflammatory bowel disease (IBD) do not meet strict diagnostic criteria due to overlap of clinical, visual and morphological data[1]. Around 80% of such patients either Crohn's disease or ulcerative colitis develops within next several years but the diagnosis remains uncertain[2]. MR enterography (MRE) benefits in assessment of bowel inflammatory lesions however insufficient bowel distention degrees decreases accuracy of MRE and its use is limited in general anesthesia patients where oral preparation is contraindicated (e.g., small children, claustrophobic and uncooperative patients) as well as in patients with contraindications to butylscopolamine administration. It is known that inflamed bowel walls presents lower apparent diffusion coefficient (ADC) values in diffusion – weighted imaging (DWI) than in intact bowel walls[3,4] but research data refer to distended bowel loops, and no data are available about ADC differences between collapsed and distended bowel walls in one and the same bowel segments.
**Aims & Methods:** The aim was to measure and compare ADC values in collapsed and distended intestinal loops of high signal intensity (SI) in DWI images in subjects without evidence of IBD as well as compare the calculated values with literature data. ADC values of collapsed and distended bowel walls with high SI in DWI images were measured in 42 patients (13–67 y.o.) with no previous diagnosis of inflammatory bowel disease (IBD) and with fecal calprotectin level $<260$ μg/g. Magnetic resonance enterography (MRE) exams were performed by 1.5 T MRI system. MRE protocol included DWI sequences with b values of 0, 100 and 600. Bowel filling was achieved with 1.51 of 2.5% mannitol orally over 40 minutes before scanning; peristalsis was reduced with butylscopolamine 20 mg intravenously. Sites of collapsed and distended jejunal and ileal loops were identified and graded as 'collapsed jejunum', 'distended jejunum', 'collapsed ileum' and 'distended ileum'. 2 ADC measurements were recorded in each of the filling grade of jejunum and ileum. Differences between filling grades within one bowel site were assessed with t-test.
**Results:** There was statistically significant difference between ADC values of collapsed and distended intestinal loops with high SI on DWI. The mean ADC values in collapsed bowel loops were lower than in distended loops subsequently being in jejunum 1.84 $mm^2/s$ ($SD = 0.54$) in collapsed state and 2.73 $mm^2/s$ ($SD = 0.60$) in distended state ($p < 0.0001$) whereas the mean ADC value in ileum for collapsed state was 2.46 $mm^2/s$ ($SD = 0.81$) and 2.89 $mm^2/s$ ($SD = 0.64$) for distended ileum ($p = 0.0075$). Comparing to the literature data ADC values in collapsed bowel loops were higher than in bowel with inflammatory changes.
**Conclusion:** The results are perspective and helpful as a control group of potentially healthy subjects and could benefit in improving diagnostic accuracy of distinction between intact and inflamed bowel loops in MRE exams of patients without bowel preparation in clinical situations where maintaining adequate bowel filling is a problem.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0826 TERMINAL ILEAL MOTILITY AS A BIOMARKER FOR CROHN'S DISEASE ACTIVITY DURING MR ENTEROGRAPHY: A PROSPECTIVE STUDY

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**Introduction:** One of the key challenges for managing Crohn's disease is knowing when to start and stop immunosuppressive medications. No single biomarker for disease activity exists although Magnetic Resonance Enterography (MRE) is increasingly implemented. The MaRIA score is a validated MRE activity score based on quantifying structural changes in the bowel associated with inflammation such as wall thickening and contrast enhancement and is considered to be one of the 'gold-standard' MRI methods for assessing disease activity[1]. However it is time consuming to use and changes with treatment often lag behind clinical response. An alternative approach is to measure small bowel motility i.e. bowel function rather than structure. Quantified motility assessment is rapid (~60 seconds per case), with previously demonstrated good inter-reader agreement[2,3]. Single site retrospective studies have suggested reduced motility is correlated with Crohn's disease activity but prospective validation is lacking.

**Aims & Methods:** This prospective study evaluates the predictive accuracy of quantified MRI small bowel motility to assess inflammatory activity in Crohn's disease against histopathological and endoscopic reference standards. Performance against conventional magnetic resonance index of severity (MaRIA) scoring is further provided for context.

82 subjects with CD (42 male, median age 32.5 years, range 16 to 70 years) were recruited prospectively from two European centres as part of the VIGOR++ study, undergoing ileocolonoscopy and MR enterography separated by median 5 days (range 0 to 14).

The CD Endoscopic Activity Index (CDEIS–endoscopic standard) was scored at the terminal ileum (TI), and a histopathological activity score based predominantly on the presence of ulceration and volume and distribution of acute inflammatory cells (eAIS–histopathological standard) was derived from multiple biopsies from the distal terminal ileum. TI motility was quantified using a validated software algorithm4 based on image registration applied to a breath hold 2D "cine" acquisition (BTFE, slice thickness 1 cm, temporal resolution 1.1 images/s).

The TI MaRIA score was calculated by two experienced readers blinded to the clinical and motility data. A motility cut-off score (0.30) was pre-selected from a prior, retrospective study5 and the sensitivity and specificity of Motility and MaRIA ($\geq$11) for disease activity (defined as eAIS $\geq$1 or CDEIS $\geq$4) calculated. Motility was correlated with reference standards using Spearman's rank and Receiver Operating Characteristic (ROC) area under the curves (AUC) were constructed. Diagnostic performance was compared using McNemar's test.

**Results:** Against eAIS, motility had sensitivity and specificity of 92.3% (95% CI 81.5–97.86%) and 75.6% (95% CI 60.4–87.1%) for activity. Sensitivity but not specificity was significantly higher than MaRIA (80.0% P = 0.03 and 79.1% P = 1.0, respectively). Against CDEIS, motility had sensitivity and specificity of 93.3% (95% CI 81.7–98.6%) and 74.0% (95% CI 60.4–85.0%), significantly higher (sens) & lower (spec) respectively than MaRIA (82% P = 0.03 and 83.7% P = 0.05). Motility had moderate negative correlations with eAIS ($R = -0.61$, $p < 0.001$) and CDEIS ($R = -0.59$, $p < 0.001$) and demonstrated a ROC AUC of 0.87 (eAIS) and 0.86 (CDEIS), respectively.

**Conclusion:** In this dual site prospective study, quantified motility appears a valid biomarker for endoscopic and histopathological activity in CD.

**Disclosure of Interest:** A. Menys: Shareholder & Director of Motilent Ltd. All other authors have declared no conflicts of interest.

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## P0827 EARLY CHANGE IN FECAL CALPROTECTIN PREDICTS PRIMARY NON- RESPONSE TO ANTI-TNFA THERAPY IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** The early identification of primary non-response to anti-TNFα therapy facilitates the timely management of patients with inflammatory bowel disease (IBD). A recent, pilot study to detect prognostic markers of early response to anti-TNFα therapy identified the two genes coding for the calprotectin subunits (S100A8, S100A9) to be among the most highly expressed gene transcripts in non-responders.

**Aims & Methods:** This retrospective study tests the hypothesis that measurements of faecal calprotectin (FCAL) pre- and post- anti-TNFα induction can predict primary non-response in both Crohn's disease (CD) and ulcerative colitis (UC). Outcomes were assessed at 6 months based on clinical activity scores and the use of corticosteroids: (a) Remission: Harvey Bradshaw Index (HBI) < 5 or SCCAI < 3, off corticosteroids > 2 months; (b) Response: drop in HBI or SCCAI > 3, off corticosteroids; (c) non-response. ΔFCAL (and ΔCRP respectively) was calculated as (FCALpost induction – FCALpre induction)*100/FCAL pre induction.

**Results:** At 6 months, 23 (72%) CD and 10 (56%) UC patients had responded. In remission were 17(53%) and 5 (28%) respectively. Comparing non-responders to combined response and remission groups, the area under the curve of ΔFCAL to predict outcomes at 6 months was 0.97 for CD and 0.96 for UC. Using ROC analysis, a Δ70% returned a sensitivity and specificity of 99% and 96%, respectively (likelihood ratio, LR = 23) in CD. For UC a Δ70% had a sensitivity and specificity of 88% and 86%, respectively (LR = 6).

**Conclusion:** A drop in FCAL < 70% after induction predicts primary non-response to anti-TNFα in both CD and UC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0828 CHARACTERISTICS OF ASYMPTOMATIC PERIANAL FISTULA IN CROHN'S DISEASE DIAGNOSED BY MAGNETIC RESONANCE IMAGING

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**Introduction:** Perianal fistula, a common complication of Crohn's disease (CD), affect up to one third of patients during the course of their disease. It is associated with significant impairment in quality of life and is an independent predictor of inflammatory bowel disease -related work disability. Mostly perianal fistula is evaluated after perianal symptoms appeared.

**Aims & Methods:** In this study, we investigated the clinical characteristics of perianal fistula in CD patients without perianal symptoms. All CD cases diagnosed initially in our hospital were evaluated perianal fistula using magnetic resonance imaging (MRI) from Oct. 2014 to Oct 2015. The medical records were studied retrospectively.

**Results:** 152 cases were categorized into three groups, 59 cases of no perianal fistula CD (NF-CD) (38.8%), 44 asymptomatic perianal fistula CD (AF-CD) (28.9%) and 49 symptomatic perianal fistula CD (SF-CD) (32.2%). Both groups of AF-CD and SF-CD showed shorter period of disease duration than that of NF-CD [12.0 (6.0,24.0) vs 24 (8, 57), P = 0.05 and 14 (6.5,24) vs 24 (8, 57), P = 0.025], higher value of hs-CRP [10.90 (10.34,11.30) vs 10.13 (3.45,11.47), P = 0.027, and 10.69 (8.94,11.44) vs 10.13 (3.45,11.47), P = 0.041], and much higher score of rectal SE-SCD [1.5 (0, 4) vs 0 (0, 3), P = 0.013 and 3 (0,4) vs 0 (0, 3), P = 0.008]. Other clinical indices of the three groups were comparable. Compared with the patients of SF-CD, those of AF-CD had more types of simple fistula (18.2% vs 4.1%, P = 0.043), more low fistula (22.7% vs 4.1%, P = 0.007), more inter-sphincteric fistula (86.3% vs 51.0%, P < 0.001), and less number of fistula (50.0% vs 75.5%, P = 0.011).

**Conclusion:** Asymptomatic perianal fistula in CD is not uncommon and should be considered when patient who has shorter disease duration, significant higher value of hs-CRP or severe rectal disease. Asymptomatic perianal fistula may be on early stage of symptomatic perianal fistula in CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0829 DERMATOLOGICAL COMPLICATIONS OF ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASE


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**Introduction:** The broader use of anti tumor necrosis factor (TNF) agents in Inflammatory Bowel Disease (IBD) has been associated to a high rate of adverse reactions. Dermatological complications are among the most common adverse reactions.

**Aims & Methods:** We assessed the cumulative incidence of dermatological complications in a large cohort of IBD patients treated with anti-TNF agents and its impact on patient's therapeutic management. A single tertiary-center observational retrospective study. All consecutive adult IBD patients treated with anti-TNF agents between 2006 and 2015 were identified. Patients who developed at least one dermatological complication while under anti-TNF therapy were included.

**Results:** Among 732 patients treated with anti-TNF agents, 211 (29%) developed at least one dermatological complication: 59% women with a mean age of $42 \pm 13$ years, 85% with Crohn's disease. Sixty-seven percent were under infliximab and 64% under combination therapy. Median follow-up time was 34 (11–71) months. Dermatological complications recorded were: infections (46.9%, 99/211), psoriasiform lesions (18.5%, 39/211), eczema and injection site reactions (16.6%, 35/211), vasculitis (5.2%, 11 / 211), neoplasias (1.9%, 4/211) and others (10.9%, 28/211). The most common cutaneous infections were bacterial (45%) and fungal (36%). Infectious complications led to a delay superior to 7 days in next dose of anti-TNF in 25 (12%) patients. Three (3%) patients with infectious complications and 12 (31%) patients with psoriasiform lesions definitely discontinued anti-TNF therapy. All patients with cutaneous malignancy discontinued therapy with anti-TNF.

**Conclusion:** Dermatological complications affected almost one-third of IBD patients treated with anti-TNF agents. Infections were the most common dermatological complication, but psoriasiform lesions induced by anti-TNF agents were the most common cause for anti-TNF therapy definitive discontinuation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0830 MR ENTEROCOLONOGRAPHY EVALUATION FOR SMALL BOWEL STRICTURES IN PATIENT WITH CROHN'S DISEASE: COMPARISON WITH BALLOON ENTEROSCOPY


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**Introduction:** Crohn's disease (CD) is a lifelong inflammatory bowel disease. Evaluating the extent and severity of the disease is critical to determine appropriate therapeutic strategies in patients with CD. Magnetic resonance (MR) enterography (MRE) / MR enterocolonography (MREC) can examine not only intra-luminal changes, but also extra-luminal abnormalities without ionizing radiation and anesthesia, which makes it appropriate for frequent examinations in CD. MR imaging is one of the most recommended technique for detection of small bowel lesions of CD. However, the accuracy for strictures in the deep small intestine is not validated.

**Aims & Methods:** The aim of this study is to evaluate the impact of stricture findings indicated by MREC and the patient outcomes using balloon-assisted enteroscopy (BAE) reference. A total of 200 CD patients with established CD were prospectively examined both MREC and BAE. Among them 75 patients were indicated strictures with BAE. The presence of strictures in the small bowel by MR was compared with endoscopic findings. Moreover, the relations between MR findings, surgical outcomes and the impact of endoscopic balloon dilation (EBD) were evaluated.

**Results:** MREC detected strictures in 45 patients (60%) and could not in 30 patients (40%). Major strictures (diameter $< 10$ mm or with internal fistula) ($p = 0.001$), long strictures ($p = 0.017$), and pre-stenotic dilatation ($p = 0.002$) were predictors of strictures detection by MREC. Surgery was observed in 16 (34%) patients with strictures both on MREC and BAE (MREC-positive-BAE-positive), on the other hand 4 (13%) patients without strictures on MREC but with strictures on BAE (MREC-negative-BAE-positive). The surgery-free rates in MR-negative-BAE-positive group were significantly lower than MREC-positive-BAE-positive group at 6 months (short-term outcome, $p = 0.008$) and 1 year (mid-term outcome, $p = 0.043$). The corresponding rates at 2 years (long-term outcome) did not differ between those groups ($p = 0.065$). In the MREC-positive-BAE-positive group, the patients who were performed with EBD showed significantly higher surgery-free rates than those who were not ($p = 0.037$).

**Conclusion:** MREC specificity for small bowel strictures was clinically sufficient; and MREC procedure could detect critical strictures, which was a predictive factor for surgical intervention. But MR-negative-BAE-positive strictures were also associated with an increased risk over 1-year follow-up.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0831 CONVENTIONAL TREATMENT REGIMENS FOR ULCERATIVE COLITIS ALLEVIATE FATIGUE – AN OBSERVATIONAL COHORT STUDY


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**Introduction:** Fatigue is increasingly recognized as an important complaint of patients with inflammatory bowel disease (IBD) (1). Optimal management of fatigue in patients with IBD is not yet known, and the course of fatigue during concentional treatment has not been widely studied in patients with ulcerative colitis.

**Aims & Methods:** The aim was to investigate potential changes in the severity of fatigue in a cohort of patients with ulcerative colitis receiving conventional drug treatment over 3 months. Furthermore to assess whether depression, disease symptoms, disease activity, and inflammatory or other selected biological markers were associated with changes in fatigue. Patients with newly diagnosed ulcerative colitis were included in an observational cohort study and received conventional non-biological drug treatment for 3 months. Colonoscopy was performed at diagnosis and after 3 months. Disease activity was assessed by Mayo score and measurement of serum C-reactive protein (CRP) and fecal calprotectin levels. Fatigue was rated using the fatigue visual analog scale (fVAS). Mood was assessed with the hospital anxiety and depression scale (HADS). Associations between fVAS scores and the variables: time, age, CRP, fecal calprotectin, hemoglobin, ferritin, Mayo scores, Mayo endoscopic scores, and HADS depression subscale (HADS-D) scores were explored.

**Results:** In the 82 included patients, median fVAS scores decreased from median (range) 40 (0–94) to 22 (0–81) after 3 months, $p = 0.001$. The prevalence of significant fatigue (defined as fVAS scores $\geq$ 50) was reduced from 40.2% to 20.7%. The fVAS scores were non-significantly lower for patients in remission compared to patients with active disease, $p = 0.13$. All disease activity markers were reduced; Mayo score from median (range) 7 (2–12) to 2 (0–11), CRP from 7 mg/L (1–117) to 1.9 mg/L (1–43) and fecal calprotectin levels, from 773 mg/kg (0–5466) to 58 mg/kg (18–2241), $p = 0.001$ for all differences. HADS-D remained unchanged from median (range) score 2 (0–10) at baseline to 1 (0–13), $p = 0.59$, whereas hemoglobin levels increased after 3 months from mean (SD) 13.7 g/L (1.5) to 14.6 g/L (1.4), $p = 0.001$. Decreased fVAS scores were associated with lower ferritin levels ($p = 0.011$), Mayo scores ($p = 0.035$) and HADS-D ($p = 0.001$) scores. There were no associations between fVAS scores and CRP, fecal calprotectin, or Mayo endoscopic scores. Colonic disease distribution did not influence fatigue significantly.

**Conclusion:** Disease activity and fatigue improved after 3 months of conventional treatment for ulcerative colitis. Over time, persistence of more severe fatigue was associated with more ulcerative colitis symptoms, but not with objective disease activity markers or colonic disease distribution. A clinical setting of standard treatment regimens and medical attention may thus alleviate fatigue in IBD patients.

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## P0832 STRUCTURAL BOWEL DAMAGE REMAINS STABLE DURING FOLLOW UP OF QUIESCENT CROHN'S DISEASE PATIENTS

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**Introduction:** Crohn's disease is associated with accumulation of progressive structural bowel damage (SBD) that may lead to stenotic or penetrating complications and frequent need for surgery. The data pertaining to the degree of progression of SBD in both active and quiescent disease is scarce. The Crohn's Disease (CD) Digestive Damage Score (Lemann Index, LI) is a novel tool for evaluation of SBD, that incorporates clinical, endoscopic and imaging data for the entire digestive tract.
**Aims & Methods: Aims:** To evaluate the progression of SBD in patients with quiescent Crohn's disease. **Methods**: Patients with known quiescent small bowel CD – for at least 3 months (CDAI < 150) were prospectively recruited and underwent repeated magnetic resonance enterography (MRE) and capsule endoscopies (CE). LI was used to assess the grade of CD-related SBD at baseline and follow-up evaluation. The gastrointestinal tract was divided to segments [esophagus, stomach, and duodenum; 20 segments for small bowel; 6 segments for colon and rectum]. Findings at MRE and CE were divided into stricturing and penetrating lesions, scored and adjusted for anatomical coefficients. Only patients who remained in clinical remission and underwent $\geq 2$ MRE evaluations were included. SBD was identified as LI > 4.8, and progression of SBD as $\Delta$ LI > 0.3.
**Results:** Fifty nine patients were enrolled; 44 remained in clinical remission and 36 underwent 2 MREs and were included in the analysis. The average interval between MRE scans was$14.8 \pm 2.5$ months.SBD was detected in 5/36 patients (13.9%) on both MRE examinations. LI was similar at baseline and follow-up ($2.6 \pm 3.7$ vs $2.5 \pm 3.8$, $p = 0.97$). There was a negligible change in LI between evaluations ($0.008 \pm 1.27$). Progression of SBD ($\Delta$LI > 03) was demonstrated in 13/36 (36.1%) and regression – in 11/36 (30.6%) of patients. Changes in SBD were not associated with biologic or immunomodulator treatment.
**Conclusion:** In patients with quiescent CD, structural bowel damage was stable, with a negligible change during a 14 months follow-up
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## P0833 RENAL INVOLVEMENT OF INFLAMMATORY BOWEL DISEASE: PROSPECTIVE STUDY

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**Introduction:** Renal involvement in chronic inflammatory bowel disease (IBD) remains an extra-digestive event that is relatively rare, occurring in 4–23% of cases. It has several aspects from simple abnormality of the urinary sediment to nephropathy and renal failure.
**Aims & Methods: Aims:** To assess the prevalence of renal disease in IBD and analyze its clinical and biological characteristics.
**Patients and methods:** Renal function (blood creatinine and creatinine clearance according to MDRD formula), the Urine culture and 24 h proteinuria were performed for 120 patients. If renal tests show abnormalities, renal ultrasound and a blood and urine electrolytes are evaluated.
**Results:** Renal involvement has been discovered in 36 patients or 30% of the cases. These are 20 women and 16 men with a sex ratio F/M of 1.25. The mean age was $40.2 \pm 13$. Ulcerative colitis was the most common, present in 19 cases (52.8%). Crohn's disease was found in 11 patients (30.5%) and indeterminate colitis in 6 cases (16.7%). Maintenance therapy was based on azathioprine for 16 patients (44.4%), salicylates for 13 patients (36%), anti-TNF and 6 Mercaptopurine for 2 patients (5.5%) respectively and methotrexate for 1 patient. The Urine culture showed a urinary infection in 9 cases (25%) and aseptic leukocyturia in 16 cases (44.4%). Crystals was found in 4 patients (13%), microscopic hematuria in 10 patients (27.7%) and macroscopic in 4 patients (11%). A positive proteinuria was found in 8 patients (22.2%). Furthermore, renal failure and kidney stones were discovered in 2 patients (5.5%) respectively.
**Conclusion:** Renal involvement during chronic inflammatory bowel disease is probably underestimated due to its silent and asymptomatic nature. Its screening must be systematic and regular to identify nephropathy in an early stage.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0834 THE ECONOMIC BURDEN OF INFLAMMATORY BOWEL DISEASE

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**Introduction:** Spiraling health-care costs are always a highly topical issue. Patients with inflammatory bowel disease are diagnosed earlier on in life and thus require a lifetime of investigations, treatment and follow-up.
**Aims & Methods:** Our aim was to calculate the economic burden of patients diagnosed with inflammatory bowel disease in 2010 in Malta. Patients diagnosed with inflammatory bowel disease on histology at endoscopy, in 2010 at Mater Dei Hospital were included in this study. Their case notes were reviewed. Costs were calculated over 5 years since diagnosis. Data was obtained for inpatient hospital stays, outpatient visits, blood tests, radiological tests, surgery, endoscopy and medications.
**Results:** 58.7% of patients had ulcerative colitis (UC). The rest (41.3%) had Crohn's disease (CD). The male to female ratio was almost 1.1. Mean age of diagnosis was 36.7 years (SD±20.9). Females were statistically more expensive to manage than males ($p < 0.019$). There was no significant statistical correlation between age at diagnosis and cost of treatment. None of this cohort required any surgical intervention. Mean cost per patient for 5 years since diagnosis were as follows:

| Cost | CD/UC | Mean (€) | Standard Deviation | Significance (P value) |
|---|---|---|---|---|
| **Inpatient stays** | CD | 1903 | 1338 | 0.254 |
| | UC | 4441 | 2811 | |
| **Outpatient visits** | CD | 399 | 197 | 0.101 |
| | UC | 301 | 187 | |
| **Blood Tests** | CD | 1021 | 480 | 0.054 |
| | UC | 708 | 576 | |
| **Imaging** | CD | 512 | 344 | 0.008 |
| | UC | 125 | 200 | |
| **Endoscopies** | CD | 1099 | 595 | 0.010 |
| | UC | 547 | 341 | |
| **Medications** | CD | 12952 | 7049 | 0.012 |
| | UC | 7831 | 5249 | |
| **Total** | CD | 16442 | 7416 | 0.005 |
| | UC | 9906 | 6939 | |

The cost of CD management per patient per year (€3288) was higher than UC (€1981). Proportion of costs in the management of inflammatory bowel disease was as follows: medications 75.3%, blood tests 6.7%, endoscopies 5.8%, inpatient stays 8.5%, outpatient visits 2.6%, imaging 1.2%.
**Conclusion:** Current trends point towards possible more aggressive medical management leading to a higher financial investment in medications rather than surgery. 5-year cost of CD was higher than that of UC across all categories except for inpatient management of UC. CD remains more expensive to treat probably due to the presence of more complicated disease requiring more investigations and use of biological drug therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0835 RISK FACTORS OF CLINICAL RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS IN CLINICAL AND ENDOSCOPIC REMISSION

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**Introduction:** Patients with ulcerative colitis (UC) in endoscopic remission have a better disease outcome with fewer complications. It has been suggested that histological features have a prognostic value in the outcome of these patients.
**Aims & Methods: Aim:** To assess the role of histology as a risk factor for clinical relapse in patients with UC in clinical and endoscopic remission. **Methods**: This was a retrospective observational study including patients with left/extensive UC who underwent a colonoscopy with biopsies between January 2005 and June 2014 and were in clinical remission (partial Mayo score 0–1, without rectal bleeding) and endoscopic remission (Mayo endoscopic subscore 0–1) while on stable treatment and free of steroids within the previous 3 months. Regarding histology, basal plasmacytosis, the presence of intraepithelial neutrophils (acute activity), the architectural alterations, and an increased mononuclear infiltrate, were evaluated. Other variables including UC flare within 12 months prior to inclusion,Mayo endoscopic subscore grade 1, biological activity (increased C-reactive protein) and treatment at the time of endoscopy, were also analysed as potential risk factors of clinical relapse. Clinical relapse was defined as the presence of symptoms together with the need for treatment optimization.
**Results:** 157 patients were included: 38% women; median age 54 years (IQR 44–65); 65% with extensive UC; 87% with Mayo endoscopic subscore = 0 and 18% presented a flare within 12 months prior to inclusion. Median time in clinical remission previous to the inclusion was 38 months (IQR 19–105) and median time of follow-up was 39 months (IQR 18–64). 31% presented clinical relapse during follow-up with a median time for relapse of 3.3 years (IQR 1.55–5.4). The cumulative probability of CR at 1, 3 and 5 years was 7%, 22% and 29%. Regarding histology: 10%, 17%, 54%, and 60% presented basal plasmocytosis, acute activity, architectural changes and mononuclear infiltrate, respectively. In the multivariate analysis (Cox), acute activity and flare within 12 months prior to inclusion showed a significant association with clinical relapse at 12 months of follow-up (RR = 7.69; 95% CI 2.03–29.05 p = 0.003-). Similar results were obtained when considering the whole follow-up period (RR = 1.97; 95% CI 1.01–3.82 p = 0.046-).
**Conclusion:** In UC patients in clinical and endoscopic remission, the presence of intraepithelial neutrophils in colonic biopsies and a shorter time of clinical remission constitute risk factors for clinical relapse. A closer monitoring is therefore recommended in these patients. Further prospective studies need to clarify whether treatment optimization is justified in this context.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0836 NO IRON AND NO ANEMIA: WHO ARE THESE CROHN'S PATIENTS AND WHAT IS THEIR EVOLUTION?

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**Introduction:** Despite many studies on anemia in Crohn's Disease (CD) exist, the knowledge about iron deficiency without anemia (IDWA) is still scarce.
**Aims & Methods:** The aim of this study was to characterize CD patients with IDWA, as well as to analyze its evolution during the follow-up. Patients with CD which have had at least one episode of IDWA between January/2011 and December/2014 were analyzed. Two subgroups were analyzed regarding the definition of iron deficiency: one group with serum ferritin $<30\mu g/L$ and no evidence of inflammation, and another group with serum ferritin between 30–$100\mu g/L$ when inflammation was evident. Besides description of the patients' evolution during the follow-up, demographic and clinical differences between the two groups were evaluated using the $\chi^2$ and Fisher's exact tests.
**Results:** From the 136 analyzed patients, 97 (71.3%) were female and the mean follow-up time was 42 ± 16 months. Regarding the evolution during the follow-up, 43 patients (31.6%) developed anemia, 51 (37.5%) resolved the iron deficiency, 35 (25.7%) had persistent IDWA, and in 7 patients (5.2%) recurrence of IDWA was confirmed after an initial period of resolution. Only 8 patients (5.9%) received iron supplementation for IDWA. There were no significant differences between the two groups regarding gender (p = 0.849), disease extension (p = 0.91) or behavior (p = 0.056), age at diagnosis (0.401), perianal (p = 0.571) or upper gastrointestinal tract involvement (p = 0.749), family history (p = 0.051) or smoking habits (p = 0.555). Although the development of anemia was not significantly different between groups (p = 0.957), resolution of IDWA was significantly more common in those patients with serum ferritin levels between 30–$100\mu g/L$ (p = 0.025).
**Conclusion:** Although about one-third of the patients with CD will have only transient IDWA, another third of the patients will develop iron deficiency anemia during the follow-up. This fact highlights the importance of the exhaustive identification and follow-up of this clinical situation, particularly in those with lower levels of serum ferritin, in which the spontaneous recuperation is not so frequent.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0837 ANORECTAL FUNCTION AND QUALITY OF LIFE IN IBD PATIENTS WITH PERIANAL DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY

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**Introduction:** Anorectal complications are a common feature of patients affected by inflammatory bowel disease (IBD) [1], with a huge impact on their quality of life (QoL) [2]. Up to now the anorectal function of IBD patients has been poorly investigated[3], with results often contrasting[4, 5]. Aim of this prospective observational study was to analyze the anorectal function and the QoL of IBD patients, and to compare the results with healthy volunteers.
**Aims & Methods:** Patients were assessed by a physical and clinical examination (including the Wexner score, the Harvey Bradshaw score, the Clinical Mayo score), anorectal manometry, three-dimensional endoanal ultrasound (3D-EAUS), and endoscopy. The patients' QoL was evaluated by administration of the Inflammatory Bowel Disease Questionnaire (IBDQ).
**Results:** From January to April 2016, 24 IBD patients (14 males; mean age 38.9 ± 12.8 years) and 20 healthy volunteers (10 males, mean age 42 ± 10.7 years) were enrolled in the study. Eighteen patients were affected by Crohn's disease (CD), and 6 by ulcerative colitis (UC), with a mean Harvey Bradshaw score and a mean Clinical Mayo score of, respectively, 6.5 ± 3.8 and 2.6 ± 2.6. Thirteen patients had a history of perianal fistula, while 7 were affected by fecal incontinence (mean Wexner score 8.6 ± 3.7). Fecal incontinent patients had a longer duration disease (p = 0.024), and a higher bowel movements number (p = 0.024). The 3D-EAUS was normal in all healthy volunteers, while 21/24 IBD patients had at least a pathological features (fistula, sphincter lesion, fibrosis). At the anorectal manometry, the maximum anal resting pressure was lower in IBD patients when compared to controls (84.9 ± 43.5 mmHg versus 128.4 ± 10.2 mmHg, p < 0.0001), while the maximum squeeze pressure was higher in IBD patients (166.8 ± 55.8 mmHg versus 122.9 ± 12.2 mmHg, p = 0.0001); the rectoanal inhibitory reflex was present in 20 out 24 IBD patients, and in all healthy volunteers; 19 out 24 IBD patients had a dyssynergic defecation pattern; rectal sensations did not differ between IBD patients and the control group. No differences emerged at the anorectal manometry between CD or UC patients, while the presence of rectal inflammation (p = 0.026) and incontinence (p = 0.040) was associated to a lower maximum anal resting pressure. Overall, the mean IBDQ score was 164.0 ± 36.7, but it was lower in UC patients when compared to CD patients (140.8 ± 44.1 versus 170.4 ± 32.9, p = ns); the score was not significantly influenced by the presence of rectal inflammation and a perianal fistula, but it was lower in patients with fecal incontinence (p = 0.030).
**Conclusion:** Anorectal function was impaired in IBD patients with perianal disease. Specific features emerged at the anorectal manometry, and should be better investigated. The perianal disease negatively affect patients' QoL.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0838 PARALLEL TEMPORAL CHANGES IN HARVEY-BRADSHAW INDEX, TNFA AND INTESTINAL FATTY ACID BINDING PROTEIN (I-FABP) IN RESPONSE TO INFLIXIMAB (REMICADE) IN CROHN'S DISEASE

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**Introduction:** Crohn's disease (CD) is characterized by increased intestinal mucosal permeability and inflammation. Unlike ulcerative colitis, CD can occur throughout the gastrointestinal (GI) tract, including the small intestine. Beyond lowering tumor necrosis factor alpha (TNFa), the ultimate biological outcome of anti-TNFa (Remicade) therapy in CD should display evidence of mucosal healing (e.g., improved mucosal epithelial integrity). Intestinal fatty acid binding protein (I-FABP) is highly and selectively expressed in the mucosal epithelium of human intestine (1) and has therefore been used as an indicator of small intestinal barrier integrity (2). It was reasoned that I-FABP might be elevated in active CD and might then serve as an indicator of mucosal healing to monitor treatment outcomes.

**Aims & Methods:** The primary aims were to determine if 1) I-FABP is elevated in active CD and 2) I-FABP parallels Remicade induced lowering of circulating TNFa and Harvey-Bradshaw Index (HBI) as a more direct indication of mucosal healing. Methods: A local biobank containing serum from 47 CD patients that underwent Remicade therapy between the years 2000 and 2004 was investigated for blood draws suitable for monitoring changes in TNFa, HBI and I-FABP. From this, serum from 11 CD patients were identified which included naive samples drawn on the first occasion of Remicade infusion (Inf1) and at two later occasions along with matching follow-up visit serum and HBI data. Remicade infusion occurred on days 1 (Inf1), 14 (Inf2) and 42 (Inf3). Follow-up visits (F1, F2 and F3) each occurred one week after infusions. Serum drawn at Inf1 was used as a reference time point to normalize data from which TNFa and HBI would be expected to decline with successful treatment. In addition to the CD patient samples, serum from 33 healthy adult subjects with normal gut permeability, assessed by lactulose:mannitol ratios $\leq$0.7 were assayed for I-FABP by ELISA (Hycult Biotech, The Netherlands). CD patient circulating TNFa was assayed by ELISA (Meso Scale Diagnostics, USA) and compared to 63 healthy subjects. Significance threshold was set as $P < 0.05$ using t-test for paired data (before and one week after treatment) or Mann-Whitney U test when comparing CD to healthy subjects.

**Results:** One of the 11 subjects (9%) was a strong outlier on several parameters and tested positive for anti-Remicade antibodies already at Inf 1. This patient was excluded, reducing sample size to $n = 10$. At Inf1, serum TNFa was 1.5 fold ($2.34 \pm 0.22$ vs $1.58 \pm 0.09$ ng/L, $P < 0.001$) and I-FABP was 2.3 fold ($2.02 \pm 0.23$ vs $0.86 \pm 0.17$ µg/L, $P < 0.001$) higher than healthy subjects. On each follow-up day, TNFa was lower than the prior infusion day as well as the subsequent Remicade infusion day, demonstrating that the drug effect was clearly identifiable in these 12–16 year old samples and was transient, returning to levels of Inf1 day by the time of next infusion. HBI values followed the same trend. TNFa and HBI were statistically significant across most time points. I-FABP also followed this trend, with F1 being statistically lower than Inf1 ($P < 0.05$) and the next two follow-ups approaching statistical significance relative their preceding infusion days ($P = 0.08$ and $P = 0.15$). Decreased I-FABP on follow-up visits was consistent in 8 out of 10 patients. Based on 3 power calculations from the I-FABP data organized as 3 independent before-after datasets, it was estimated that a sample size of 25 CD patients is desirable to obtain significance ($P < 0.05$) for all 3 follow-up visits relative preceding infusion days. Combining I-FABP data for all 3 infusion days into one group and all follow-ups into a second group ($n = 30$) yielded a significant difference ($P < 0.005$).

**Conclusion:** Despite concerns about stability partly stemming from its short half-life in blood (~10 min), I-FABP was clearly higher in CD than healthy controls with a magnitude comparable to TNFa in biobank samples stored over 12 years. A parallel drug effect of Remicade on TNFa, HBI and I-FABP was found. I-FABP may be useful to monitor treatment progress at the level of mucosal epithelial barrier integrity.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0839 MONITORING BONE MINERAL CONTENT WITH BY BIOIMPEDANCE ANALYSES AMONG ANTI-TNF TREATED INFLAMMATORY BOWEL DISEASE PATIENTS

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**Introduction:** Patients suffering from inflammatory bowel diseases (IBD) are risked to have abnormal body composition. Altered body composition can affect body fat, muscle mass and bone mineral content as well. The risk of decreased bone mineral density content and osteopenia related bone fracture is well known among IBD patients. Tumor necrosis factor inhibitors has a known beneficial effects to bone turnover in rheumatoid arthritis patients, however its not prowed in IBD.

**Aims & Methods:** Our study involved 40 IBD outpatients (33 Crohn's disease, 7 ulcerative colitis); 24 of these received adalimumab (160/80/40 mg every other week) and 16 were treated with infliximab (5 mg/kg at week 0, 2, 6, and subsequently every 8 weeks). Body composition and bone mineral content was measured by bioelectrical impedance analysis (BIA) with an InBody 720 device. The screening was recorded prior to initiating biologicals and 3, 6 and 12 months afterwards. Baseline bone mineral content was recorded with DEXA and laboratory parameters related to bone metabolism were measured at the induction phase of biologicals.

**Results:** At the end of the 12 months observational period, 27 of 40 patients were on biologicals. Baseline bone mineral content measuerd by BIA imporved significantly during the follow up time (month 0, 3, 6 and 12: $2.90 \pm 0.62$ kg; $2.99 \pm 0.68$ kg; $2.95 \pm 0.61$ kg; $2.95 \pm 0.64$ kg; $p < 0.05$, respectively). We also observed significal improvement in total mineral content ($3.54 \pm 0.75$ kg; $3.63 \pm 0.82$ kg; $3.59 \pm 0.74$ kg; $3.59 \pm 0.80$ kg; $p < 0.05$; resp.) and in body cell mass parameter ($34.04 \pm 7.97$ kg; $35.11 \pm 8.24$ kg; $34.80 \pm 7.68$ kg; $34.60 \pm 8.47$; $p < 0.05$; resp.). At the end of induction therapy bone metabolism related laboratory parameters improved as well ($\beta$-crosslaps: $561.00 \pm 302.30$ pg/ml vs. $530.30 \pm 381.48$ pg/ml; $p < 0.05$; osteocalcin: $27.43 \pm 16.78$ ng/ml vs. 36.77 vs. 25.93 ng/ml; at week 0 and 12, resp.)

**Conclusion:** Significant improvement was observed in bone parameters measured by BIA during anti-TNF therapy among IBD patients. Our finding suggests that biompedance analyses may have a role in follow up of bone mineral content as it is less expensive and more easily accessible than other methods.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0840 ANTI-TNF-INDUCED PSORIASIS IN INFLAMMATORY BOWEL DISEASE: A 10-YEAR EXPERIENCE

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**Introduction:** Anti-tumor necrosis factor (TNF)-alpha agents are widely used for the treatment of both inflammatory bowel disease (IBD) and psoriasis. Paradoxically, anti-TNF therapy has been associated to the development of psoriasis in IBD patients, which may lead to treatment discontinuation.

**Aims & Methods:** We analysed all cases of psoriasis induced by anti-TNF therapy in a large cohort of IBD patients and assessed its impact on patients' therapeutic management. A retrospective observational study of IBD patients treated with infliximab or adalimumab between 2006 and 2015. IBD patients who developed psoriasis while under treatment with ant-TNF agents were included. Patient's characteristics, duration and type of anti-TNF therapy, lesions characteristics and outcome were analysed.

**Results:** Among 732 IBD patients, 39 (74% women, mean age $38 \pm 11$ years) developed anti-TNF induced psoriasis (cumulative incidence 5.3%). Thirty-seven (95%) had Crohn's disease, 49% were under adalimumab and 51% under infliximab. Median time until the diagnosis of psoriasis after starting anti-TNF agent treatment was 15 (IQR 4–26) months. The most common lesions were plaque psoriasis (51%) or inverse psoriasis (28%) and the most frequent rash location was palmoplantar (31%), scalp (28%) or trunk (26%). Fifty-one percent of patients improved with topical treatment and 49% required systemic therapy (PUVA or methotrexate). Two (5%) patients switched anti-TNF agent but there was a severe recurrence of lesions in both cases, thus anti-TNF therapy was definitely discontinued. Globally, 31% of the patients permanently discontinued therapy with clinical improvement in 81% of cases.

**Conclusion:** The cumulative incidence of anti-TNF induced psoriasis in this large cohort of IBD patients was 5.3%. Half of the patients had a favourable response to topical therapy, but in almost 1/3 of the patients it was necessary to permanently discontinue anti-TNF therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0841 ETROLIZUMAB TREATMENT DOES NOT MODIFY LEVELS OF VCAM-1 IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** Etrolizumab, an anti-$\beta$7 monoclonal antibody, targets the integrins $\alpha4\beta7$ and $\alpha E\beta7$ and inhibits the interaction of $\alpha4\beta7$ with MAdCAM-1 and VCAM-1, and $\alpha E\beta7$ with E-Cadherin. IBD patients have higher levels of expression of MAdCAM-1 and ICAM-1 in the gut tissue compared to controls. Expression levels of VCAM-1 (Jones, 1995; Panés, 2003), an adhesion molecule

**Abstract No: P0842**

**Table:** Summary of PMS response and PMS remission by treatment group over time (A), and at Wk 2 as predictors of efficacy endpoints at Wk 8 (B)

| A. | | Wk 2 | Wk 4 | Wk 8 |
|---|---|---|---|---|
| **PMS response, n (%)** | | | | |
| Tofacitinib 10 mg BID (N = 905) | | 488 (53.9)*** | 603 (66.6)*** | 625 (69.1)*** |
| Placebo (N = 234) | | 74 (31.6) | 98 (41.9) | 102 (43.6) |
| **PMS remission, n (%)** | | | | |
| Tofacitinib 10 mg BID (N = 905) | | 193 (21.3)*** | 308 (34.0)*** | 391 (43.2)*** |
| Placebo (N = 234) | | 23 (9.8) | 38 (16.2) | 46 (19.7) |
| **B.** | **Proportion of subjects at Wk 8, n (%)** | **Predictor at Wk 2** | **Sensitivity - Specificity** | **Odds ratio (95% CI)** |
| Clinical response | 521 (57.6) | PMS response | 72.2–75.5 | 8.0 (6.1, 10.4)+++ |
| | | PMS remission | 31.5–94.7 | 8.2 (5.4, 12.4)+++ |
| Mucosal healing | 271 (29.9) | PMS response | 73.3–59.3 | 4.0 (3.0, 5.3)+++ |
| | | PMS remission | 40.3–88.8 | 5.3 (3.9, 7.3)+++ |
| Remission | 159 (17.6) | PMS response | 85.0–57.0 | 7.5 (4.9, 11.6) +++ |
| | | PMS remission | 56.6–87.8 | 9.4 (6.6, 13.4) +++ |

Patients with missing data were treated as non-responders.***$p < 0.0001$ vs placebo, based on the Cochran-Mantel-Haenszel chi-square test stratified by study, prior treatment with tumour necrosis factor inhibitors, corticosteroid use at baseline and geographic region, used to test the treatment difference between tofacitinib 10 mg BID and placebo in PMS remission and PMS response.+++$p < 0.0001$, based on the chi-square test for the association between predictor at Wk 2 and clinical outcome at Wk 8.BID, twice daily; CI, confidence interval; PMS, partial Mayo score; Wk, week.

involved in cell trafficking across the blood-brain barrier, are reported to be similar between IBD patients and controls. We demonstrated that etrolizumab treatment in patients with moderate-to-severe ulcerative colitis (UC) modulates MAdCAM-1 and E-Cadherin in serum and colonic tissue (Vermeire, 2014; Fuh, 2015; unpublished data) whereas natalizumab has been shown to decrease serum VCAM-1 in multiple sclerosis patients (Millonig, 2010).

**Aims & Methods:** The aims of this study were to explore the role of etrolizumab treatment on VCAM-1 and ICAM-1 serum levels and expression in colonic tissue among patients in the Phase 2 EUCALYPTUS study. Phase 2 UC patients were randomized into one of 3 different treatment arms during an induction period of 10 weeks: placebo (n = 36), 100 mg dose (n = 28), and 300 mg dose (n = 34). Soluble VCAM-1 and ICAM-1 were measured at baseline and during the treatment period using commercially available ELISA assays and tissue expression was assessed in biopsy tissue by qPCR.

**Results:** No differences were observed in serum soluble VCAM-1 and ICAM-1 levels between etrolizumab-treated arms and the placebo arm. Similar results were observed in VCAM-1 expression in colonic tissue on Day 43 and Day 71. In colonic biopsies, there was no dose-proportional decrease of ICAM-1 expression in the etrolizumab-treated arm. However, levels of ICAM-1 expression in colonic tissue of clinical responders, in both etrolizumab- and placebo-treated arms, decreased significantly compared with non-responders at Day 43; in etrolizumab-treated responders/remitters, this reduction was maintained through Day 71. There were no consistent differences in VCAM-1 expression in colonic biopsies between placebo-treated responders and non-responders or between etrolizumab-treated remitters, responders and non-responders.

**Conclusion:** Lack of changes in VCAM-1 levels in both colonic tissue and serum is consistent with the mechanism of action of etrolizumab which does not block interaction of $\alpha 4\beta 1$ with VCAM-1. The observed downmodulation of ICAM-1 expression is likely due to a decrease in tissue inflammation and not to direct targeting of the pathway. These and prior data indicate that etrolizumab modulates expression of gut-specific MAdCAM-1 and suggests that it does not affect lymphocyte trafficking to CNS via VCAM-1 modulation. Funded by Genentech.

**Disclosure of Interest:** F. Fuh: Full-time employee of Genentech Inc., a member of the Roche Group.
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S. Vermeire: Consult.: AstraZeneca, Ferring; grant/research support, MSD, Takeda, AbbVie; advisory committees/review panels: Ferring, MSD, Pfizer, Shire, AbbVie, Mundipharma, Hospira, Takeda, Genentech Inc.; speaker fees: Ferring, MSD, Pfizer, AbbVie, Hospira, Takeda
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## P0842 ONSET OF EFFICACY OF TOFACITINIB FOR INDUCTION THERAPY IN PATIENTS WITH ACTIVE ULCERATIVE COLITIS IN TWO MULTINATIONAL, PHASE 3 CLINICAL TRIALS


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**Introduction:** Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). Two Phase 3 randomised placebo-controlled studies (OCTAVE Induction 1, NCT01465763; OCTAVE Induction 2, NCT01458951) demonstrated efficacy of tofacitinib 10 mg twice daily (BID) vs placebo as induction therapy for patients with moderate to severe UC.[1]

**Aims & Methods:** We investigated how response and remission based on partial Mayo score (PMS) at Week (Wk) 2 correlate with clinical efficacy endpoints at Wk 8. Patients in both studies were randomised (4:1) to receive treatment with tofacitinib 10 mg or placebo BID for up to 9 wks. Patients were ≥18 years old with moderately to severely active UC defined at baseline by Mayo score of ≥6, rectal bleeding subscore ≥1 and endoscopic subscore ≥2. Patients had previous failure or intolerance to treatment with ≥1 of corticosteroids, thiopurines, or tumour necrosis factor inhibitors (TNFi). Primary endpoint was remission at Wk 8 defined as Mayo score ≤2, no subscore >1 and rectal bleeding subscore of 0. Secondary endpoints included clinical response (decrease from baseline Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1) at Wk 8, mucosal healing (Mayo endoscopic subscore ≤1) at Wk 8 and PMS at Wks 2, 4 and 8. Exploratory endpoints included PMS response (PMS ≥2 decrease from baseline) and PMS remission (PMS ≤2 with no individual subscore >1 at Wks 2, 4 and 8). The chi-square test was used to test whether PMS response and remission at Wk 2 correlated with remission, mucosal healing and clinical response at Wk 8. Sensitivity was defined as the proportion of patients who achieved Wk 2 PMS response or PMS remission among Wk 8 responders. Specificity was defined as the proportion of patients who did not achieve PMS response or PMS remission at Wk 2 among Wk 8 non-responders.

**Results:** Treatment difference with tofacitinib 10 mg BID vs placebo was achieved at Wks 2, 4 and 8: of 905 patients treated with tofacitinib 10 mg BID, 53.9%, 66.6% and 69.1% achieved PMS response, and 21.3%, 34.0 and 43.2% achieved PMS remission at Wks 2, 4 and 8, respectively (Table A). Both PMS response and PMS remission, at Wk 2, were significantly associated ($p < 0.0001$) with all three clinical efficacy endpoints: clinical response; mucosal healing; and remission at Wk 8 (Table B). Similar results were obtained in both subpopulations of TNFi-naïve and -experienced patients.

**Conclusion:** In patients with moderate to severe UC treated with tofacitinib 10 mg BID, tofacitinib demonstrated induction efficacy based on PMS as early as Wk 2, the first time point measured in this study. Efficacy at Wk 2 is a good predictor of efficacy at Wk 8, regardless of prior TNFi therapy. Patients who have not achieved remission or response at Wk 2 based on PMS may still achieve improvements in Mayo score at Wk 8.

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S. Danese: Speaker, consultant, advisory board member: Boehringer Ingelheim, Merck & Co, Ferring, TiGenix, Millenium Takeda, Pharmacosmos, Genentech, Grunenthal, Pfizer, AstraZeneca, Novo Nordisk, Cosmo Pharmaceuticals, Vifor, Johnson and Johnson

J. Panés: Consultant: AbbVie, Boehringer Ingelheim, Ferring, Galapagos, Genentech-Roche, GSK, Pfizer Inc, Second Genome, Takeda, TiGenix, Topivert
H. Zhang: Employee and shareholder: Pfizer Inc
D. Woodworth: Employee and shareholder: Pfizer Inc
A. Marren: Employee and shareholder: Pfizer Inc
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### P0843 ETROLIZUMAB TREATMENT MODULATES MADCAM-1 LEVELS IN SERUM IN ULCERATIVE COLITIS PATIENTS

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**Introduction:** Etrolizumab, an anti-$\beta7$ monoclonal antibody that targets the integrins $\alpha4\beta7$ and $\alpha E\beta7$, has shown efficacy in patients (pts) with moderate-to-severe ulcerative colitis (UC). Serum drug levels in etrolizumab-treated pts from the Phase 2 EUCALYPTUS study demonstrated linear kinetics in drug exposure. Target engagement was measured as receptor occupancy (RO) by flow cytometry; complete RO was observed at the time of initial assessment at Day 5 after the first dose in both dose cohorts (Vermeire, 2014).
**Aims & Methods:** The aim of this study was to assess the relationship between drug levels and RO with levels of MAdCAM-1, the ligand for $\alpha4\beta7$, in the serum of EUCALYPTUS pts. Pts enrolled in the EUCALYPTUS study were randomized (1:1:1) into 3 different treatment arms: a 100 mg etrolizumab dose cohort (100 mg at week 0, 4, and 8), a 300 mg dose cohort (loading dose of 420 mg at week 0 and 300 mg at week 2, 4 and 8) or a placebo control. The study included a treatment period of 10 weeks (last dose given on week 8) followed by 18 weeks of safety follow-up/drug wash-out. Biomarker data was analysed from 112 pts (n = 40 placebo, n = 34 at 100 mg, and n = 38 at 300 mg + loading dose).
**Results:** Serum analysis indicated a gradual and significant decrease from baseline of soluble MAdCAM-1 in etrolizumab-treated pts (mean ± SE, day 5: –19 ± 4%, day 29: –67 ± 3%) with no significant changes observed in the placebo arm. There were no apparent dose-dependent differences in the decrease of soluble MAdCAM-1 levels in the two etrolizumab arms. After the last dose at week 8, during the wash-out phase, a decrease in serum drug concentration levels (to < 1 μg/mL) was associated with a loss of RO, and concurrent increase in soluble MAdCAM-1. Baseline levels of MAdCAM-1 did not predict etrolizumab responses, and post-dose levels did not correlate with clinical responses or remission to etrolizumab treatment.
**Conclusion:** Etrolizumab-treated UC pts demonstrated a significant decrease in serum MAdCAM-1 compared to placebo. While the drop in soluble MAdCAM-1 was not correlated with response, nor did baseline levels of soluble MAdCAM-1 predict responses to treatment, the decrease in serum MAdCAM-1 levels can potentially be used as a surrogate for RO. In the Phase 2 study, the $\alpha E$ component of $\alpha E\beta7$ was identified as a biomarker that may predict responses to etrolizumab treatment. Further work in the Phase 3 studies will explore biomarkers predictive of responses to etrolizumab treatment. Funded by Genentech.
**Disclosure of Interest:** F. Fuh: Full-time employee of Genentech Inc., a member of the Roche Group.
R. Erickson: Full-time employee of Genentech Inc., a member of the Roche Group.
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M. Keir: Full-time employee of Genentech Inc., a member of the Roche Group.
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T. Ramirez Montagut: Full-time employee of Genentech Inc., a member of the Roche Group.

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### P0844 DEVELOPMENT AND ANALYTICAL CHARACTERIZATION OF GP2017, A PROPOSED ADALIMUMAB BIOSIMILAR

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**Introduction:** As many of the biologic agents used to treat inflammatory bowel diseases will lose patent protection during the next few years, biosimilars are becoming an increasingly important focus of development. The demonstration of biosimilarity is based on the evaluation of all physicochemical, biological, nonclinical and clinical data; i.e. the totality of the evidence.[1] For new drugs, the major goal is to describe the product analytically and then determine clinical properties. By contrast, the overall aim of biosimilar development is to prove that the biosimilar and originator product contain essentially the same active substance, and confirm the expectation that both products will elicit the same clinical effects. Since analytical tools are a highly sensitive means of comparing two products, comprehensive physicochemical and biological characterization of the proposed biosimilar and originator product serves as the foundation of the overall comparability exercise.
**Aims & Methods:** The aim of this study is to describe the techniques and approaches used to characterize and compare the physicochemical and structure-function properties of GP2017, a proposed adalimumab biosimilar, with its originator product. Multiple batches of the originator were sourced and analyzed using state-of-the-art analytical methods to define the development target for GP2017. A manufacturing process was iteratively designed and modified to develop a product with quality attributes and biological function within the predetermined variability ranges of the originator. GP2017 and the originator were analyzed with respect to primary and higher-order structure as well as post-translational modifications. Binding of GP2017 and the originator to recombinant tumor necrosis factor-$\alpha$ (TNF$\alpha$) and a panel of human Fc$\gamma$ and FcRn receptors was analyzed using surface plasmon resonance-based assays. Cell-based bioassays were used to compare levels of TNF$\alpha$ neutralization, binding of membrane-bound TNF$\alpha$, complement-dependent cytotoxicity, antibody-dependent cellular cytotoxicity and apoptosis.
**Results:** Multiple orthogonal analytical methods showed similarity between GP2017 and the originator. The amino acid sequences of GP2017 and the originator were identical, protein folding was indistinguishable and post-translational modifications including glycosylation, C-terminal variants, methionine oxidation and deamidation were also similar. At the in vitro level, the binding affinity of GP2017 to TNF$\alpha$ was within the predetermined variability range of the originator. Binding affinities of GP2017 to the tested panel of receptors were similar to the originator and both products had similar bioactivity in terms of cytotoxicity and apoptosis inhibition.
**Conclusion:** The observed physicochemical and functional similarity between GP2017 and the originator, as part of the totality of the evidence, demonstrate that the biological component of both products is essentially the same active substance. GP2017 is therefore a suitable candidate to move into the next stages of biosimilar development; i.e. nonclinical, pharmacokinetic and confirmatory clinical studies.
**Disclosure of Interest:** M. Schiestl: Paid employee of Sandoz GmBH
C. Roesli: Paid employee of Hexal AG

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### P0845 SUSTAINED RESOLUTION OF EXTRAINTESTINAL MANIFESTATIONS IN PATIENTS WITH CROHN'S DISEASE RECEIVING ADALIMUMAB

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**Introduction:** Extraintestinal manifestations (EIMs) in patients (pts) with Crohn's disease (CD) are associated with morbidity and impaired quality of life.[1] This analysis evaluated effects of adalimumab (ADA) on median time to first recurrence of EIMs following initial resolution in pts with EIMs; predictors of initial resolution and sustained resolution (time to first recurrence of EIMs) were also assessed.
**Aims & Methods:** EIM data were pooled from 11 open-label (OL) or double-blind induction, maintenance, and OL extension studies in adult and pediatric pts with CD (age 13–17 years old). The ADA group included pts who received blinded or rescue OL ADA in randomised trials and those who received OL ADA in non-randomised trials. The placebo (PBO) group included pts randomised to PBO, including those who received OL ADA induction before randomisation to PBO. Data from PBO pts who received OL ADA rescue therapy after randomisation were censored from that point. In 10 studies, question 4 of the Crohn's Disease Activity Index was used to evaluate EIMs at scheduled and unscheduled visits; in 1 study, a separate form was used. Sustained resolution, defined as median time to first recurrence following initial resolution, was calculated for any EIM and for musculoskeletal EIMs (arthritis/arthralgia). A log-rank test was used for between-group comparison. A Cox model was used to determine predictors of resolution (data from 10 studies) and sustained resolution (data from 11 studies) in pts with any EIM or with arthritis/arthralgia.
**Results:** For pts with EIMs at baseline who achieved resolution, sustained resolution was significantly longer for the ADA group vs the PBO group for any EIM ($P < 0.001$) and for musculoskeletal EIMs ($P < 0.001$; **Table 1**).

**Table P0846**

| Patient | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Age (yrs), Gender | 33, f | 51, m | 57, m | 21, m | 50, m | 47, f | 32, m | 21, m | 50, m | 23, m |
| Primary Diagnosis | PSC | PSC | PSC | AISC | PSC | PSC | AISC | AISC | AISC | PSC |
| Age at OLT (yrs) | 20 | 40 | 52 | 20 | 48 | - | - | - | - | - |
| IBD extent | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis | pancolitis |
| Disease duration (yrs) | 10 | 5 | 25 | 6 | 15 | 1 | 10 | 7 | 4 | 1 |
| Duration of IBD pre-OLT (yrs) | Post | Post | 20 | 5 | 13 | | | | | |
| Immunosuppression | Tac | Tac, MMF, Pred | Tac | Pred | Aza, Tac, Pred | Pred | Aza | | | |
| , Pred | Pred | | | | | | | | | |
| , MMF | Pred, Aza | Mercap | | | | | | | | |
| Prior Anti-TNF use | Yes | Yes | Yes | Yes | No | Yes | Yes | No | Yes | No |
| Time from OLT to VDZ (yrs) | 13.3 | 10.8 | 4.2 | 0.9 | 1.6 | - | - | - | - | - |
| SCCAI | 7 | 8 | 7 | 12 | 10 | 6 | 5 | 9 | 3 | 4 |
| Mayo endoscopy score | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 2 |
| Duration of VDZ (m) | 10.8 | 7.3 | 13.4 | 5.1 | 4.1 | 4.4 | 7.1 | 1.4 | 8.7 | 7.4 |
| Maintenance therapy | Yes | Yes | Yes | Yes | Yes | Yes | Yes | No | Yes | Yes |

Predictors of resolution for any EIM were: ADA treatment (P = 0.003), younger age (P < 0.001), moderate (vs severe) disease activity at baseline (P < 0.001), lower baseline levels of albumin (P = 0.013), and higher baseline levels of C-reactive protein (CRP; P = 0.026). Predictors of resolution for arthritis/arthralgia were the same except for CRP (P = 0.052). Predictors of sustained resolution for any EIM were ADA treatment (P < 0.001), male sex (P = 0.031), and shorter disease duration (P = 0.010). Predictors of sustained resolution for arthritis/arthralgia were ADA treatment (P < 0.001), younger age (P = 0.050), and shorter disease duration (P = 0.029).

**Table 1:** Median Time to First Recurrence of Any EIM and Musculoskeletal EIMs Following Initial Resolution

| | | Time to First Recurrence | | |
|---|---|---|---|---|
| EIM | Treatment group (n) | Median, d | 95% CI | P |
| Any EIM | PBO (137) | 57 | 43–70 | <0.001 |
| | ADA (848) | 136 | 113–169 | |
| Musculoskeletal (arthritis/arthralgia) | PBO (130) | 57 | 36–71 | <0.001 |
| | ADA (808) | 141 | 113–169 | |

**Conclusion:** ADA treatment was effective for achieving sustained resolution of EIMs in pts ≥13 years old with CD. ADA treatment and shorter disease duration were among the predictors of sustained resolution for any EIMs and musculoskeletal EIMs.

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R. Löfberg: R. Löfberg has received research grants from Sophiahemmet and the Stichting af Jochnick Foundation and lecture and consultancy fees from Abbott and other companies.
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D. Schwartz: D. Schwartz has received grant support from AbbVie and UCB; and consultancy fees from AbbVie, UCB, Janssen, Takeda, and Tigenix.
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## P0846 VEDOLIZUMAB IN INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH AUTOIMMUNE LIVER DISEASE PRE- AND POST-LIVER TRANSPLANTATION: A CASE SERIES

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**Introduction:** Inflammatory bowel disease (IBD) associated with primary and autoimmune sclerosing cholangitis (PSC and AISC respectively) appears to represent a distinct clinical entity in comparison to 'classical' ulcerative colitis (UC) and Crohn's disease (CD). The course of IBD appears to be influenced by liver transplantation (LT): typically following an indolent course pre-LT, while an aggressive phenotype may be seen in up to 50% of patients post-LT and de novo disease reported in up to 25%. Anti-TNF therapy can be efficacious but systemic complications remain a real concern, while evidence for other therapeutic interventions is limited to pre-clinical models and small case series. Vedolizumab (VDZ), a humanised monoclonal antibody directed against the $\alpha 4\beta 7$ integrin is appropriate for induction and maintenance of remission of moderate to severe IBD, either naïve or refractory to anti-TNF agents. In this case series, we report our experience of VDZ for patients with PSC/AISC-IBD pre- and post-LT.

**Aims & Methods:** Patients were identified from a prospectively kept database at 2 tertiary hospitals. The diagnosis of liver disease was based on established diagnostic criteria and confirmed with a liver biopsy in all patients. IBD clinical activity was assessed using the Simple Clinical Colitis Activity Index (SCCAI) at baseline and end of follow-up (as all patients had only colonic involvement and were therefore classified as ulcerative colitis for the purposes of this report). A clinical response was defined as a drop in SCCAI > 3 with remission defined as a total score < 3. Quality of life (QoL) was assessed by the IBD-control-8 questionnaire. Faecal calprotectin (FCAL) and endoscopic activity (Mayo endoscopic sub-score) are also provided.

**Results:** Ten patients were identified with PSC/AISC-IBD. Table 1 summarises the disease characteristics and outcomes. There were 7 (70%) with previous primary or secondary non-response to anti-TNF agents. The median interval between LT and initiation of VDZ therapy was 4.2 (1, 13) years. Five patients were on corticosteroids for active IBD before induction (median dose 40 [20–40] mg/day) and were successfully weaned in 4/5 (80%). Surgery was required for one patient during induction due to acute severe colitis. The median duration of VDZ therapy in the 9 patients who received maintenance was 7.4 [1.4–12.5] months. Overall a clinical response was seen in 4/10 (40%) one of whom achieved clinical remission (sustained to last follow-up). In responders, a drop in faecal calprotectin (μg/g; median 708 [60–2696] vs. 90 [32–960], p = 0.03 by Wilcoxon test) and improvement in QoL scores were observed [5 (0, 13) vs. 13 (8, 16), p = 0.03]. Abnormalities in liver biochemistry were seen in two post-LT patients, but both had recurrence of their liver disease prior to VDZ initiation. No infective complications were attributed to VDZ use. There were no malignancies identified during the follow-up period.**Conclusion:** This is the first case series of VDZ use in PSC/AISC-IBD patients pre- and post-LT. Therapy has been well tolerated by all patients and no safety signals have been identified during the follow-up period despite concomitant immunosuppresants. VDZ shows promise as a safe and efficacious treatment in PSC/AISC-IBD, even in the post-LT setting. As experience increases, taking into account its potential beneficial effects for autoimmune liver disease as well as the infectious complications associated with anti-TNF use, it seems likely that VDZ will become the treatment of choice for IBD in this patient group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0847 PREGNANCY OUTCOMES IN WOMEN EXPOSED TO INFLIXIMAB (INNOVATOR)

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**Introduction:** Rheumatologic, dermatologic and inflammatory bowel disorders (IBD) can affect women of childbearing potential. Infliximab ([IFX], Innovator) is approved for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC) and psoriasis (PsO). To characterize pregnancy outcomes in patients treated with IFX (Innovator), data obtained from maternal exposure to IFX (Innovator) are presented.

**Aims & Methods:** Dataset includes individual patient cases within the company safety database through 23 August 2015. Cases originated from various sources, including spontaneous reporting, clinical studies, and registries. Cases include prospectively reported (ie, pregnancy outcome not known when first reported) maternal exposures to IFX (Innovator) during pregnancy or within 2 months prior to conception with a known pregnancy outcome in RA, PsA, AS, CD, UC, or PsO pts. Birth outcome was stratified by grouped indication.

**Results:** 1362 prospective pregnancy reports with reported outcomes (103 in RA, PsA, and AS; 1023 in IBD (CD & UC); 33 in PsO) were identified. Mean maternal age was 29.7 years. Of the 1362 pregnancy reports, 1115 (81.9%) resulted in live births, 147 (10.8%) in spontaneous abortion (SA), 72 (5.3%) in elective/induced abortion, 12 (<1%) in abortion scheduled, 1 (<1%) in unspecified abortion, 9 (<1%) in ectopic pregnancy, 3 (<1%) in C-section, 1 (<1%) in molar pregnancy and 2 (<1%) in still births. Of the 1115 live births, 25 (2.2%) congenital anomalies (CA) and 85 (7.6%) preterm births were reported (Table). Of the 1362 prospective pregnancy reports, 695 (51%) reported first trimester (T1) exposure to IFX (Innovator). Among 695 reports of the T1 IFX (Innovator)-exposure, 592 (85.2%) pregnancies resulted in live births, 68 (9.8%) in SA, 23 (3.3%) in elective/induced abortion, 4 (<1%) in abortion scheduled, 3 (<1%) in ectopic pregnancy, 3 (<1%) in C-section, 1 (<1%) in molar pregnancy, and 1 (<1%) in still birth. Of the 592 pregnancies resulting in live births with T1 IFX (Innovator)-exposure, 11 (1.9%) CA and 40 (6.8%) preterm births were reported (Table). In characterizing the reports by indication, the percentage of CA among live births was 7.1% (6/84) in rheumatological indications, 1.8% (15/832) in IBD, and 0% (0/23) in PsO. The average maternal age for the rheumatological indications was 30.5 years.

**Table:** Summary of pregnancy reports with known outcomes in patients treated with IFX (Innovator) for RA, PsA, AS, CD, UC and PsO

| Pregnancy Outcome | All IFX (Innovator)-exposed pregnancies n, (%) | T1 IFX (Innovator)-exposed pregnancies n, (%) |
|---|---|---|
| Total no of reports with known outcome | 1362 | 695 |
| Live birth | 1115 (81.9) | 592 (85.2) |
| Congenital anomalies | 25 (2.2) | 11 (1.9) |
| Preterm birth | 85 (7.6) | 40 (6.8) |
| Abortion | | |
| Spontaneous | 147 (10.8) | 68 (9.8) |
| Elective/Induced | 72 (5.3) | 23 (3.3) |
| Scheduled | 12 (<1) | 4 (<1) |
| Unspecified | 1 (<1) | 0 |
| Ectopic pregnancy | 9 (<1) | 3 (<1) |
| Still birth | 2 (<1) | 1 (<1) |
| C-section | 3 (<1) | 3 (<1) |
| Molar pregnancy | 1 (<1) | 1 (<1) |

**Conclusion:** Pregnancy outcomes among pregnancies with T1 IFX (Innovator)-exposure did not differ from the pregnancy outcomes among all prospectively reported pregnancies exposed to IFX (Innovator). Higher percentages of CA were reported among rheumatological indications in comparison to IBD and PsO. The combined rate of CA among pregnancies with IFX (Innovator) exposure was comparable to US general population (3%)[1]. Potential confounders will be further characterized. Limitations of this analysis include lack of a direct comparison group and missing data in the reports.

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## P0848 CROHN'S DISEASE (CD) PATIENTS WITH HIGH BODY MASS INDEX PRESENT MORE FREQUENT AND RAPID LOSS OF RESPONSE TO INFLIXIMAB

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**Introduction:** Infliximab (IFX), a tumor necrosis factor (TNF) antagonist, is effective in patients with luminal and perianal Crohn'sdisease (CD) (1). Nevertheless, up to 40% of patients with an initial response to IFX lose the benefit within the first year. Excess of fat tissue may have pharmacological effects on TNF antagonists. The aim of our study was to determine whether the body mass index (BMI) affects response to IFX during the first year of treatment in CD patients.

**Aims & Methods:** We performed a retrospective and observational study at a tertiary referral center including all luminal CD patients who started IFX between January 2010 and May 2014. BMI was calculated before initiation of IFX and patients were divided into 3 groups according to the WHO BMI categories: BMI $< 25\,kg/m^2$ (normal BMI), $25\,kg/m^2 \leq BMI \leq 30\,kg/m^2$ (overweight) and BMI $> 30\,kg/m^2$ (obesity). The following data were recorded during the first year of follow-up: optimization of IFX treatment, delay of IFX optimization, rate of mucosal and/or morphological healing, occurrence of an intestinal resection surgery, introduction of corticosteroid (CT) and/or immunosuppressant (IS) therapy and IFX treatment withdrawal. The occurrence of one of the three previous events (occurrence of surgery, CT or IS introduction, and IFX withdrawal) was considered as a pejorative event. A descriptive statistical analysis was performed on the population selected, including median calculation and range interquartile for the continuous data and percentages for discrete variables. The independence between two variables was investigated by the chi square test. Student's test was performed for comparison between groups.

**Results:** One hundred and forty patients were included, with 21 patients (15%) overweight and 23 patients (16%) obese. The median BMI at baseline was $22\,kg/m^2$. Characteristics ill introducing IFX were comparable between the three groups (phenotype and location of the CD diagnosis according to the Montreal classification, clinical activity Disease score according to the Harvey Bradshaw, CRP, and existence of IS treatment at the introduction of IFX). At 12 months from the beginning of IFX treatment, the rate of IFX optimization was significantly higher in overweight and obese patients than in the normal BMI group: 48%, 44% and 20% respectively ($p = 0.0002$). Furthermore, the optimization period was significantly shorter in these same patients: 8.5, 8, 17 months respectively ($p = 0.03$). There was no significantly difference between overweight and obese patients regarding the rate and time optimization IFX ($p = 1.0000$ and $p = 0.93$ respectively) and there was no significant difference between the three groups concerning the others parameters.

**Conclusion:** We report the first study demonstrating a loss of response to IFX more frequent and faster in obese and overweight CD patients. These Results suggest that these types of patients justify an IFX induction with higher doses and close control of residual IFX concentrations.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0849 OUTCOMES OF EMERGENCY ADMISSIONS WITH ULCERATIVE COLITIS IN ADULTS IN ENGLAND BETWEEN 2004 AND 2014

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**Introduction:** Between 2008 and 2014, the UK national audit of adult ulcerative colitis (UC) admissions revealed a fall in mortality from 1.54 to 0.75%, a rise in anti-TNF therapy in steroid non-responders from 12 to 43%, and a fall in emergency surgery from 12 to 11%.

**Aims & Methods:** Hospital Episode Statistics (HES) is an administrative database of data on all elective and emergency care episodes in hospitals in England. Using HES, patients aged between 18 and 60 years coded with a first emergency admission with UC were identified. The influence of demographic factors, comorbidity and infused anti TNF therapy on mortality, surgery and emergency readmissions was examined using multivariate logistic regression.

**Results:** Between 2004 and 2014, 17,344 patients (47.5% female and mean age of 36 (IQR 26–45)) were identified. Mortality was 0.13% at 30-days, 0.17% in hospital and 0.55% within 1 year. During admission, 11.5% of patients had surgery (median time to surgery 6 days (IQR 1–17)) and 1.93% had infused anti-TNF therapy. Surgery during admission fell non-significantly from 12.4 to 11.7% between 2004 and 2014, but the fall in surgery within a year between 2004 and 2013 was significant (OR 0.65 (95% CI 0.52–0.83) $p < 0.001$). Anti-TNF therapy rose from 0.9 to 4.6% between 2006 and 2014. In-hospital and 1 year mortality fell from 0.25 and 0.69% in 2004 to 0.14 and 0.56% in 2014 but this was not statistically significant. Patients aged 35–60 had a higher in-hospital (3.69 (1.37–9.94) p 0.010) and 1-year mortality (2.68 (1.66–4.33) $p < 0.001$) than those aged 18–34. Increased comorbidity was associated with 30-day mortality (29.73 (9.89–89.41) $p < 0.001$) and non-white patients had a lower 1-year mortality (0.59 (0.38–0.92) $p = 0.010$). Females were less likely to have surgery during admission (0.67 (0.61–0.74) $p < 0.001$) or within 1 year (0.87 (0.79–0.96) $p < 0.001$), but gender was not associated with mortality. Patients aged 35–60 (1.17 (1.06–1.29) p 0.001) and those of non-white ethnicity (1.27 (1.12–1.42) $p < 0.001$) were more likely to have surgery during admission. Patients given anti-TNF therapy during admission were more likely to need surgery at the time (1.40 (1.03–1.89) $p = 0.031$) and within 1 year (1.44 (1.04–2.00) $p = 0.030$). Emergency readmissions within 30 days were associated with younger age (35–60 years 0.89 (0.81–0.97) $p = 0.011$) and increased comorbidity (1.78 (1.22–2.62) $p = 0.003$).

**Conclusion:** For patients with a first emergency admission for UC, there was no change mortality between 2004 and 2014. Rates of anti-TNF therapy during emergency admission have increased and surgery decreased over time. Older men and non-white ethnicity were associated with surgery during admission and the use of anti-TNF agents was associated with an increased risk of surgery, likely reflecting severe colitis.

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All other authors have declared no conflicts of interest.

## P0850 SYSTEMATIC REVIEW – MANAGEMENT OF CHRONIC REFRACTORY POUCHITIS IN ADULTS UNDERGOING RESTORATIVE PROCTOCOLECTOMY WITH ILEOANAL POUCH ANASTOMOSIS FOR ULCERATIVE COLITIS

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**Introduction:** Restorative proctocolectomy (RPC) with ileal pouch anal anastomosis (IPAA) is considered the procedure of choice in patients with ulcerative colitis (UC) refractory to medical therapy. This approach is popular amongst patients since it restores intestinal continuity and avoids the necessity for a long-term stoma. The incidence of pouchitis is 20% at one year and up to 40% at 5 years. 10 to 15% of patients with pouchitis experience chronic pouchitis, which is classified as either 'treatment responsive' or 'treatment refractory'. Often in refractory unresponsive pouchitis trial medications have been utilized, usually unlicensed. This review summarises the 19 trials looking at the treatment of chronic pouchitis and builds on the cochrane review in 2015 which summarised the 2 randomised control trials in the management of chronic pouchitis.

**Aims & Methods:** Aims: To determine the efficacy of various oral and topical medical therapies for the treatment of chronic refractory pouchitis in patients undergoing IPAA for ulcerative colitis. Methods: A computer-assisted search of MEDLINE and EMBASE was carried between 1966 and February 2016 by two independent researchers. Manual searches of the reference list from the potentially relevant studies were performed in order to identify additional studies that may have been missed using the computer-assisted search strategy. Abstracts from conferences were also manually searched from 1965–2016 in order to identify unpublished studies. Outcomes: The proportion of patients with clinical improvement or remission of pouchitis. Remission was defined according to individual study and remission endpoints ranged from 15 days to 10 weeks. Chronic pouchitis was defined differently in each study with the majority defining it as symptoms for at least 4 weeks despite either antibiotics or steroid therapy.

**Results:** The literature search identified a total of 2954 studies. Two authors (JPS and NSD) independently reviewed the titles and abstracts of these studies. After screening 16 were included in the study. 4 additional papers were included after manual reference searching. A total of 19 papers were considered eligible. Antibiotics: Low-quality evidence suggests that tinidazole and ciprofloxacin were better than mesalazine in inducing remission in chronic pouchitis but not significantly, rifaxamin and ciprofloxacin for 15 days had an 33% success rate at achieving remission in chronic pouchitis and combination of metronidazole 400 mg or 500 mg twice daily and ciprofloxacin twice daily for 28 days had an 82% remission rate. Low-quality evidence also supports that metronidazole was significantly better than placebo at decreasing stool frequency. Steroids: Low-quality evidence suggests that oral beclomethasone 5 mg once daily for 8 weeks then tapered by 5 mg every 2 weeks until suspension can induce remission in 80% of patients and budesonide induced remission in 75% of patients. Biologics: Pooling low-quality evidence suggests that infliximab can induce remission in 21/50 (42%) at 1 year and 12/24 (50%) at 10 weeks using infliximab. Adalimumab at 10 weeks had a remission rate of 5/7 71% at 10 weeks. Tacrolimus: Pooling low-quality evidence suggests that tacrolimus in both enema form and tablet form may have benefit in achieving remission for chronic pouchitis. Tacrolimus: enemas induced clinical remission with significant reductions in PDAI at 8 weeks. Other Therapies: Low-quality evidence suggests that alicaforsen enemas at week 6, can induce remission in 7/12 patients (58%). Other treatments such as faecal transplantation, elemental diets did were not able to induce remission significantly in the above literature

**Conclusion:** The treatment of chronic refractory pouchitis remains difficult and is largely empirical. Our knowledge of the treatment of this condition is based on small studies with often poor study designs and small numbers. There may be room for larger multi-centre trials in order to generate larger study populations and therefore more meaningful data. There is also room for larger randomised control trials to aid the management of chronic refractory pouchitis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### Reference

1. Extensive Reference list available on request.

## P0851 INFLIXIMAB-TNF COMPLEXES DETERMINE THE APPEARANCE OF ANTI-DRUG ANTIBODIES

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**Introduction:** Anti-drug antibodies (ADA) may hamper infliximab (IFX) efficacy. Factors determining the appearance of ADA in some but not all individuals are still poorly understood. It has been suggested that ADA formation is triggered by low drug levels in the serum, yet no clear causality was hitherto demonstrated.

**Aims & Methods:** We aimed to define whether exposure to low IFX level triggers ADA formation and investigate whether other factors are related to immunogenicity. To test this, C57BL/6 mice received intra-peritoneal IFX injection in escalating doses. Serum drug levels (SDL) and ADA level were measured using ELISA. To test whether a rapid decrease of IFX levels rather than low levels per se triggered ADA formation, human TNF (hTNF) was injected intra-venously in escalating doses after administration of a fixed IFX dose, allowing for IFX-hTNF complex formation. SDL, IFX-hTNF complexes and ADA were measured. Evidence for IFX-TNF complexes in human tissue of IFX-treated patients was sought utilizing a novel ELISA.

**Results:** In mice, SDL correlated well with injected IFX dose. Two weeks after IFX injection, all mice in the higher IFX dose group developed ADA, while no ADA were detected in mice injected with the lower dose. SDL predicted ADA formation (AUC 0.748 (CI 0.657–0.839), $P < 0.0001$) and SDL of $>9.35\,\mu g/ml$ was 9.2 times more likely to produce positive ADA than SDL $<9.35\,\mu g/ml$ (OR 9.2, CI 3.43–24.81, $P < 0.0001$). Repeated low IFX dose injections every 2 weeks did not elicit any ADA response. Human-TNF injection after IFX elicited a rapid decline in SDL and appearance of measurable IFX-hTNF complexes, followed by boosted ADA appearance in all mice a week thereafter. IFX-hTNF complex level strongly predicted ADA (AUC 0.944 (CI 0.851–1.000), $p = 0.003$). Injection of mice with in-vitro formed IFX-hTNF complexes elicited similar in-vivo robust ADA formation. In-vitro stoichiometric experiments with different IFX/hTNF ratios (3:2 to 3:0.01) confirmed propensity for IFX-hTNF complex formation. Various IFX-hTNF complex sizes were demonstrated by western blotting. Finally, IFX-TNF complexes were found in human intestinal tissue of IFX-treated patients.

**Conclusion:** Higher IFX doses were more immunogenic in C57BL/6 mice. The presence of IFX-hTNF complexes boosted ADA appearance in mice and their presence was demonstrated in human intestinal tissue. Stochastic formation of IFX-TNF complexes may explain the variable time course of ADA formation in IFX-treated patients depending of IFX/TNF ratios.

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All other authors have declared no conflicts of interest.

## P0852 GO-COLITIS 6-WEEK INDUCTION PATIENT-REPORTED OUTCOMES OF PARTIAL MAYO SCORE RESULTS

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**Introduction:** Patient-reported outcomes (PROs), such as the stool frequency and rectal bleeding components of the partial Mayo score, have received increasing attention as important treatment goals for ulcerative colitis (UC).[1–4] GO-COLITIS is a multicentre, open-label, single-arm, phase 4 study (NCT02092285; 2013–004583–56) that measured efficacy of subcutaneous golimumab (GLM) in anti-TNF-$\alpha$–naïve UK patients with moderate to severe UC despite conventional treatment. Results of the PROs of the partial Mayo score from the 6-week induction phase are presented here.
**Aims & Methods:** Adults with UC ≥3 months, moderate to severe disease (partial Mayo score 4–9 or Mayo score 6–12) at baseline (BL), Mayo rectal bleeding subscore ≥1, and Mayo endoscopy subscore ≥2 (if full Mayo was used) were included. Patients received GLM on day 0 (200 mg) and day 14 (100 mg) during the 6-week induction phase, followed by GLM 50 mg or 100 mg every 4 weeks during the 48-week maintenance phase as per the Summary of Product Characteristics, with 12-week follow-up. Measurements taken at BL and week 6 included the PRO components of the Mayo score.
**Results:** Overall, 205 patients were enrolled (mean [range] age, 39.3 [18–79] years; male, n = 123 [60%]) and received one (n = 2) or two doses (n = 203) of induction GLM. This resulted in pronounced improvements from BL to week 6 in the stool frequency (mean change, –1.1; SD, 1.0), rectal bleeding (mean change, –1.1; SD, 0.9), and physician global assessment (mean change, –1.1; SD, 0.9) subscores of the Mayo score (all $P < .0001$). Improvements in stool frequency and rectal bleeding subscores included increased proportions of patients with normal scores and decreased proportions with severe scores at week 6 versus BL (**Table**).

| | Baseline (n = 205) | Week 6 (n = 198) |
|---|---|---|
| Stool frequency | | |
| Normal | 3 (1.5%) | 54 (27.3%) |
| 1–2 stools more than normal | 16 (7.8%) | 61 (30.8%) |
| 3–4 stools more than normal | 64 (31.2%) | 40 (20.2%) |
| 5 or more stools more than normal | 122 (59.5%) | 43 (21.7%) |
| Rectal bleeding | | |
| No blood seen | 6* (2.9%) | 111 (56.1%) |
| Streaks of blood with stool less than half the time | 77 (37.6%) | 57 (28.8%) |
| Obvious blood with stool most of the time | 94 (45.9%) | 24 (12.1%) |
| Blood alone passed | 28 (13.7%) | 6 (3.0%) |

*Protocol violations, but included in primary analysis.

**Conclusion:** During the GO-COLITIS induction phase, patients with moderate to severe UC experienced significant improvements from BL to week 6 in the PROs of the partial Mayo score. These changes parallel the significant improvements found in the physician global assessment and patient-reported quality of life (EQ-5D/IBDQ) at week 6 versus BL.[5] The rectal bleeding and stool frequency PROs of the Mayo score could thus be a simple and noninvasive way for patients with UC to monitor their response to treatment in daily clinical practice.
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G. Gillespie: Employee of MSD
C. Wheeler: Employee, Shareholder: MSD, Consulting Fees: MSD, Roche, Takeda, Johnson and Johnson, Sanofi, Abbvie, Gilead, GSK Shareholder: GSK, Shield Therapeutics, Newlink Genetics, Oncomed, Ark Therapeutics, Verastem
All other authors have declared no conflicts of interest.

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## P0853 GUT MICROBIOTA OFFERS UNIVERSAL BIOMARKERS FOR INFLAMMATORY BOWEL DISEASE ACTIVITY EVALUATION AND TREATMENT OUTCOME PREDICTION

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**Introduction:** A global rise in the prevalence of inflammatory bowel disease has been reported, especially in countries with previously low incidence rates, such as China. Inflammatory bowel disease is associated with an imbalance in gut microbiota, including reduced bacterial diversity and Firmicutes abundance. The gut microbiota differs among human populations because of variation in genetic polymorphisms, diet, lifestyle, and environmental conditions.
**Aims:** This study was performed to identify gut microbiome patterns in a Chinese population with inflammatory bowel disease (IBD) and to investigate if any specific gut microbiome markers are associated with the activity of IBD and the response to infliximab treatment. Methods: We enrolled 51 Chinese patients with ulcerative colitis (UC), 72 with Crohn's disease (CD) and 73 healthy volunteers as control (HC) for cross-sectional comparison of gut microbiota using stool samples. Gut microbial communities were profiled by sequencing the 16S rRNA V4 region. These data were analyzed and compared with Givers's RISK cohort and PRISM cohort to investigate cross-cohorts and cross-ethnics microbial patterns associated with IBD. Furthermore, 16 CD patients were treated with infliximab (IFX) for 30 weeks and their faecal microbiota patterns were analyzed before and after treatment.
**Results:** Compared to healthy controls, IBD patients showed increased abundance of *Actinobacteria*, *Proteobacteria*, *Bacilli*, *Veillonella*, *Granulicatella*, *Enterococcus*, *Lactobacillus*, *Streptococcus*, *Rothia*, *Morganella* and decreased abundance of *Firmicutes*, *Turicbacter*, *Coprococcus*, *Lachnospira*, *Roseburia*, *Faecalibacterium*, *Ruminococcus*, *Phascolactobacterium* and *Clostridiales*. Increase in Actinobacteria and Proteobacteria and decrease in Firmicutes were strongly correlated with CD and UC severities ($p < 0.05$). Comparison to the RISK and PRISM cohorts suggests that patterns of gut microbiome dysbiosis are universal in IBD patients despite the ethnic and region differences. The predictive modelling of IBD diagnosis performs well across cohorts and ethnics groups. For IFX-treated CD patients, gut microbiota showed restored diversity as well as a significant increased trend of Clostridiales abundance in the reponse group (n = 9), compared with those in the relapse group (n = 7). Using a machine learning model including mainly two orders of Clostridiales and bacteroidales, the microbiota alone can predict the treatment outcome to 86.5% accuracy.
**Conclusion:** Gut microbiota offers potential but universal biomarkers for early diagnosis of IBD, disease activity evaluation and IFX-treatment outcome prediction, which may pave the way to the usage of gut microbiota to stratify IBD patients and apply personalized treatment for optimal outcomes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0854 EFFICACY AND SAFETY OF GRANULOCYTE, MONOCYTE/MACROPHAGE ADSORPTIVE APHERESIS IN STEROID-DEPENDENT ACTIVE UC WITH INSUFFICIENT RESPONSE OR INTOLERANCE TO IMMUNOSUPPRESSANTS AND/OR BIOLOGICAL THERAPIES (THE ART TRIAL): CALPROTECTIN AND ENDOSCOPY RESULTS

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**Introduction:** Treatment options in steroid-dependent, chronic-active ulcerative colitis (UC) with insufficient response or intolerance to immunosuppressants and/or biologicals are limited. The ART trial intended to document efficacy and identify refractory UC subpopulations which could benefit from Granulocyte/Monocyte adsorptive (GMA) apheresis (Adacolumn®). At week 12, clinical remission and response rates were 37.2% and 53.2% respectively (ITT Population; N = 95) [1]. We report final calprotectin and endoscopy results which objectively substantiate the reported clinical remission and response rates at Week 12 and Week 24.

**Aims & Methods:** This was a prospective multicenter cohort trial conducted in the UK, France and Germany. 95 patients (18–75 years) with steroid-dependent active UC (Clinical Activity Index (CAI) $\geq$ 6; Endoscopic Activity Index (EAI) $\geq$ 4) and insufficient response or intolerance to immunosuppressants (IS) and/or TNF inhibitors were included. Patients received at least 5 and up to 10 GMA aphereses in a single induction series over up to 10 weeks. Primary endpoint was the clinical remission rate (CAI $\leq$ 4) at week 12. We calculated the proportions of patients with calprotectin above and below cut-offs of 200, 250, 300, 400 and 600 mg/kg at Weeks 12 and 24, as well as EAI subscores using McNemar's test in the ITT population at week 12.

**Results:** Logistic regression analyses did not show correlation of remission or response at 12 weeks to age, gender, duration of disease, previous failed anti-TNF, previous failed immunosuppression, baseline steroid intake, number of apheresis used or smoking status. 94% of patients had calprotectin values above the reference range at Baseline. Median values decreased from Baseline (890.5) to Week 12 (555.0) and further to Week 24 (492.5; median difference: 221.0 [95% CI: −461, −52.0]). All 95% Confidence Intervals excluded zero, indicating statistically significant changes from Baseline. 25% and 39.2% of patients achieved calprotectin levels $<$200 mg/kg at Week 12 and Week 24, respectively. Statistically significant decreases for calprotectin were found comparing baseline to Week 12 at cut-off values 200 mg/kg [p = 0.0325]; 300 mg/kg [p = 0.0412] and 600 mg/kg [p = 0.0164]; as well as at Week 24 at cut-off values 200 mg/kg [p = 0.0003]; 300 mg/kg [p = 0.0105] and 600 mg/kg [p = 0.0124]; respectively. Results for the PP Population demonstrated a similar pattern. Mean EAI at Baseline was 8.7; the mean change at Week 12 was −2.2 [95% CI: −3.0, −1.4] for the ITT Population and −2.5 [95% CI: −3.4, −1.7] for the PP Population. All 95% CIs excluded zero, indicating statistically significant changes from Baseline. Statistically significant decreases were subsequently found for EAI subscores Granulation scattering reflected light, [p = 0.0029]; vulnerability [p $<$ 0.0001] and mucosal damage [p = 0.0003] at week 12 in the ITT population. Better EAI results in the PP population paralleled CAI improvement in PP by number of apheresis sessions applied [p $<$ 0.05].

**Conclusion:** We describe a cohort of steroid-dependent moderate to severe active UC patients with failure or intolerance to previous treatment with IS and/or anti-TNF, treated with GMA apheresis induction therapy. Clinical benefit was seen in over 50% of patients at week 12. This is paralleled by a statistically significant improvement of mucosal damage parameters Calprotectin and EAI subscores. GMA apheresis may be a safe alternative treatment option in UC patients with failure or intolerance to immunosuppressants and TNF-inhibitors.

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A. Akbar: A.A. received honoraries and fees as investigator and advisory board member from Otsuka Pharamaceutical Europe Ltd.
B. Bonaz: B.B. has received honoraries as investigator and advisory board member from Otsuka Pharmaceutical Europe, Ltd.

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## P0855 VEDOLIZUMAB PROVIDES CLINICAL BENEFIT OVER ONE YEAR IN PATIENTS WITH REFRACTORY INFLAMMATORY BOWEL DISEASE – RESULTS OF A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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**Introduction:** Vedolizumab (VDZ), a humanized monoclonal antibody against the $\alpha4\beta7$-integrin is effective in inducing and maintaining remission in Crohn's disease (CD) and ulcerative colitis (UC). The aim of this study was to determine 54-week efficacy of VDZ in inflammatory bowel disease (IBD) patients in a real-world clinical setting.

**Aims & Methods:** This observational, multicenter registry from 6 academic, 2 community centers and one IBD practice assessed real-world clinical outcome data for IBD patients newly treated with VDZ. The primary endpoint was clinical remission (CR) (CD HBI $\leq$ 4/UC pMayo $\leq$ 1 without rectal bleeding) at week 54. Secondary endpoints included week 30 and 54 clinical response (HBI / pMayo score drop $\geq$3) and steroid-free remission.

**Results:** A total of 127 adult patients with CD (n = 67, median HBI 9 (5–30)) or UC (n = 60, median pMayo 6 (5–9)) were analyzed. Only 9.0% of CD and 18.3% of UC patients were anti-TNF naïve. At week 54, 20.9% of CD patients and 25.0% of UC patients achieved CR (all based on non-responder imputation). If CD patients did not respond to VDZ or UC patients did not enter CR by week 14, probability of CR at week 54 was 7% and 10%, respectively. Clinical remission at week 54 was significantly more frequent in anti-TNF naïve UC patients (OR 5.250 (1.277–21.583) or patients without steroid dependency (OR 11.762 (1.403–98.630)). Decline of CRP or fecal calprotectin values predicted 54-week remission in UC. VDZ treatment was stopped in 69/127 patients (56.4%) (median week 18 (range 2–49)). Lack of response was the main reason for discontinuation of VDZ. Most common AEs were arthralgia, nasopharyngitis and fatigue.

**Conclusion:** VDZ was clinically effective in 20–25% of initially enrolled patients, who continued treatment beyond induction therapy and were in clinical remission after one year. A better substance specific patient stratification – as earlier treatment of anti-TNF-naïve or steroid independent patients – may enhance VDZ efficiency in every-day clinical practice.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0856 PATTERNS OF DOSE ESCALATION AMONGST PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE TREATED WITH VEDOLIZUMAB VS. INFLIXIMAB IN THE UNITED STATES (US)

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**Introduction:** The infliximab (IFX) label in the US recommends dose escalation (DE) for patients with Crohn's disease (CD) who initially respond and then lose response. Vedolizumab, a monoclonal antibody to the $\alpha4\beta7$ integrin was approved for use in patients with moderately-to-severely active ulcerative colitis (UC) and CD in May 2014 with a maintenance dosing regimen of 300 mg every 8 weeks. This study investigated the proportion of UC and CD patients who experience maintenance DE of vedolizumab (VDZ) vs. IFX in a real-world clinical practice setting in the US.

**Aims & Methods:** This retrospective cohort study used data from 1/6/2014 – 3/11/2015 in the US Explorys Universe electronic health records database. Adult patients with $\geq$ 12 months of available medical history, diagnosed with UC (ICD-9-CM 556.xx) or CD (ICD-9-CM 555.xx), and who received $\geq$ 5 infusions (including 3 for induction and $\geq$ 2 for maintenance) of VDZ or IFX were included. The 1st observed infusion defined the index date. Given that 8 weeks (56 days) is the standard maintenance dosing schedule, DE was defined as occurring when a patient received $\geq$ 2 maintenance infusions during an interval of 7–52 days since last infusion. DE was assessed at 180 days and 210 days after treatment initiation and results were stratified by prior biologic use.

**Results:** Among 101 VDZ and 228 IFX patients who qualified for the 180-day analysis, the mean age was 43 years for VDZ and 44 years for IFX and the proportion of females was 60.4% in VDZ and 50.4% in IFX. DE during 180 days was statistically significantly lower in VDZ compared with IFX (4.0% VDZ vs. 21.5% IFX, $P < 0.05$). Among 71 VDZ and 27 IFX with prior biologic treatment, DE was 5.6% VDZ and 25.9% IFX, $P < 0.05$. Among those without a prior biologic, DE was 0% VDZ and 20.9% IFX, $P < 0.05$. Among 96 VDZ and 213 IFX patients who qualified for the analysis of DE during 210 days, DE was observed in 5.2% VDZ and 25.8% IFX, $P < 0.05$. Among 68 VDZ and 24 IFX with prior biologic treatment, DE was 5.9% VDZ and 29.2% IFX, $P < 0.05$. Among those without a prior biologic, DE was 3.6% VDZ and 25.4% IFX, $P < 0.05$.
**Conclusion:** Results from this US database study suggest that a higher proportion of IBD patients with prior biologic treatment experienced DE than those without. In addition, patients treated with VDZ were less likely to experience DE than patients treated with IFX. This could, in part, reflect the guidance in the US IFX label to increase the dose for patients with CD who initially respond and then lose response.
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M. Luo: Employee of Takeda Pharmaceuticals, USA.
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## P0857 THE EFFECTIVENESS OF TREATMENT OF PATIENTS WITH LUMINAL FORM CROHN'S DISEASE MESENCHYMAL STROMAL CELLS OF THE BONE MARROW – 7 YEARS OF OBSERVATION

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**Introduction:** Anticytokine therapy with anti-TNF-alpha drugs contributes to the achievement of stable remission of Crohn's disease (CD). For the treatment of CD are also using mesenchymal stromal cells (MSCs). **Objective:** To examine the long-term efficacy (7 years) therapy mesenchymal stromal cells (MSCs) from the bone marrow of patients with luminal Crohn's disease (CD).
**Aims & Methods:** 80 patients with luminal form CD (terminal ileitis, colitis and ileokolit) were divided into two groups. The first group of patients aged 19 to 58 years old (Me-29) (n = 34) received the culture of MSCs under the scheme (0–1–2–3, then every 26 weeks). The second group of patients with CD (n = 46) aged 20 to 62 years (ME-28) received standard anti-inflammatory therapy with 5-aminosalicylic acid (5-ASA), glucocorticosteroids (GCS) and immunosuppressive (IS). Evaluation of the effectiveness of therapy on the level of the index of activity of Crohn's disease (CDAI < 150 point) was carried out at 12, 24, 36, 48, 60, 72 and 84 months after initiation of therapy.
**Results:** Among the patients in 1st group relapse in the 12 months of observation occurred in 4/36 patients (11.76%). In 2nd group, relapse occurred in 5/46 (10.8%) (p = 0.82). After 24 months in the 1st group of patients receiving MSC, relapse occurred in 6/34 (17.6%). In the 2nd group of patients relapse in 19/27 (41.3%) (p = 0.044). After 36 months in 1st group patients with a relapse of the disease in 11/34 (32.3%). In the 2nd group relapse 29/46 (63.1%) (p = 0.01). After 48 months in 1st group, receiving MSCs, relapsed in 15/34 (44.1%). In the 2nd group relapse in 33/46 (71.7%) (p = 0.023). After 60 months in the 1st group relapse in 19/34 (55.9%). In the 2nd group relapse 40/46 (86.9%) (p = 0.004). After 72 months in 1st group relapse 25/34 (73.5%). In 2nd group relapse of the CD in 45/46 (97.8%) (p = 0.001). After 84 months in 1st group relapse CD in 29/34 (85.3%). In the 2nd group of patients CD relapse occurred in 46/46 (100.0%) (p = 0.011).
**Conclusion:** MSCs transplantation helps to maintain a long-term clinical remission in patients with luminal Crohn's disease compared with GCS/IS therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0858 POSTOPERATIVE INFECTIOUS COMPLICATIONS IN CROHN'S DISEASE: RESULTS FROM PRACTICROHN STUDY

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**Introduction:** Crohn's disease (CD) surgery is related to postoperative complications in 11 to 14% of all cases. Infectious complications (ICs) are the most common. The aim of this study is to describe the prevalence and factors associated with the ICs in a cohort of patients with CD.
**Aims & Methods:** PRACTICROHN was a study that included patients aged ≥18 years-old from 26 centers who underwent CD-related ileocolonic or ileorectal resection with ileocolonic or ileorectal anastomosis between January 2007 and December 2010. Clinical data and treatments, including surgery was retrospectively collected from medical records. Analyzed ICs were: intra-abdominal abscess, wound infection, catheter-related sepsis and extra-abdominal infections.
**Results:** 364 patients were analyzed (mean age 32 years [SD13], 50% men). Median time from CD diagnosis to surgery was 6 years (IQR 1–12). Indication for surgery was: stenosing (n = 169, 48%), penetrating (n = 114, 45%), penetrating + stenosing (n = 51, 14%) and resistance to treatment (n = 21, 6%). 69 patients presented some IC (18%), with a hospitalization median of 19 days IQR (10–30) vs 9 days IQR (7–12) in patients without IC ($p < 0.001$). The most frequent IC were wound infection (n = 33, 28%) and abscess (n = 28, 24%); extra-abdominal infections (n = 12, 10%) and infections of the catheter (n = 4, 3%). None of them were associated with mortality. ICs were more frequent in patients in which perforation was the reason for surgery (n = 11, 39% vs n = 27, 20% p = 0.048). No differences in ICs were observed related to age, gender, smoking habit location or length of intestinal resections. No treatment was correlated with a higher rate of ICs. Table 1.

| Treatment received | No IC | IC | p |
|---|---|---|---|
| Corticosteroids, n(%) | 70 (24.48) | 20 (29.85) | 0.452 |
| Immunosuppressants, n(%) | 133 (45.70) | 32 (47.76) | 0.866 |
| Anti-TNF, n(%) | 49 (16.84) | 15 (22.39) | 0.372 |

**Conclusion:** One in five patients who underwent a CD related surgery presented some postoperative IC, being perforation the most related cause of surgery associated with these complications. None of the treatments were associated with the presence of ICs.
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C. Romero: full time employee for MSD Spain
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## P0859 ABP 501, A PROPOSED BIOSIMILAR TO ADALIMUMAB: FUNCTIONAL SIMILARITY ADDS TO THE TOTALITY OF EVIDENCE IN SUPPORT FOR BIOSIMILARITY IN ALL APPROVED INDICATIONS OF USE

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**Introduction:** ABP 501 is being developed as a biosimilar candidate to adalimumab. Demonstration of biosimilarity requires totality of evidence based on a step-wise approach, starting with structural and functional characterization followed by toxicology and pharmacokinetic (PK) assessments. A clinical study confirms efficacy, safety, and immunogenicity. Extrapolation may allow a biosimilar to be labeled for use in indications for which the reference product is approved but the biosimilar has not been studied in the biosimilarity clinical trials. Evidence from analytical[1] and PK comparisons[2] indicates that ABP 501 is similar to adalimumab. Results of two phase 3 studies have confirmed clinical similarity[3,4]. Adalimumab exerts its effects by binding tumor necrosis factor-α (TNFα) and inhibiting pro-inflammatory signaling; this is the primary mechanism of action for all indications. Additional mechanisms may play a role in inflammatory bowel diseases (IBD), such as binding to cell surface membrane-bound TNFα (mbTNFα) or through Fc-mediated effector functions. To support extrapolation to IBD, specific functional studies explored similarity of ABP 501 to adalimumab in these mechanisms.
**Aims & Methods:** Binding of ABP 501 and adalimumab to soluble TNFα (sTNFα) and mbTNFa were tested. Blocking of TNFα-induced caspase activation and IL-8 secretion and blocking of lymphotoxin-α (LTα; TNFβ) bioactivity (ie, specificity) were also assessed. To confirm similarity in Fc-mediated functions, antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC) were tested, as was inhibition of proliferation in a mixed lymphocyte reaction (MLR). Multiple lots of ABP 501, adalimumab sourced from the United States (US) and adalimumab sourced from the European Union (EU) were compared.
**Results:** The mAbs similarly bind sTNFα [108% mean relative binding for ABP 501, 111% for adalimumab (EU), 112% for adalimumab (US)] and similarity is also demonstrated in neutralization of sTNFα activity and specificity against LTα. These assessments reflect on signaling outcomes important to all indications. Binding to mbTNFα is similar [103% mean relative binding for ABP 501, 106% for adalimumab (EU), 105% for adalimumab (US)] and functionally adalimumab and ABP 501 similarly inhibit proliferation in an MLR. Similarity in ADCC [85% mean relative activity for ABP 501, 87% for

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**Table:** Market share (M/S) of biosimilar infliximab in five European countries in 2015

| | France | Germany | Spain | UK | Italy |
|---|---|---|---|---|---|
| **Biosimilar price per vial (€) (RP price per vial (€))** | 434.4 (434.4) | 551.9 (580.1) | 402.2 (536.3) | 478.2 (531.3) | 428.01 (570.68) |
| **Q1 M/S %*** | **0.0** | **2.0** | **4.4** | **0.1** | **0.3** |
| **Q1 Biosimilar vials sold (RP vials sold)** | **67(180,614)** | **2,440(122,429)** | **3,508(80,640)** | **132(112,194)** | **169(61,601)** |
| **Q2 M/S %** | **0.7** | **9.2** | **15.5** | **3.6** | **6.5** |
| **Q2 Biosimilar vials sold (RP vials sold)** | 1,246 (179,752) | 10,765 (117,254) | 11,379 (73,474) | 4,130 (113,978) | 3,616 (55,392) |
| **Q3 M/S %** | **5.8** | **12.5** | **17.4** | **11.8** | **15.7** |
| **Q3 Biosimilar vials sold (RP vials sold)** | 10,684 (183,970) | 14,879 (118,625) | 12,974 (74,506) | 13,248 (112,136) | 8,554 (54,523) |
| **Q4 M/S %** | **10.7** | **17.2** | **22.7** | **25.3** | **28.8** |
| **Q4 Biosimilar vials sold (RP vials sold)** | 19,272 (180,538) | 19,964 (116,291) | 16,695 (73,585) | 26,023 (102,941) | 14,247 (49,419) |

*M/S for biosimilar infliximab = (biosimilar infliximab vials sold/RP vials sold) × 100%

adalimumab (EU), 86% for adalimumab (US)] and CDC [100% mean relative activity for ABP 501, 94% for adalimumab (EU), 94% for adalimumab (US)] is also demonstrated.

**Conclusion:** The totality of evidence shows that ABP 501 is similar to adalimumab in multiple functional assessments, including of mbTNFα-mediated activities that have been suggested to be important for efficacy in IBD. These results, along with previous analytical, PK, and clinical similarity results, provide support for ABP 501 extrapolation to all approved adalimumab indications.

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S. Kuhns: Amgen employee and stockholder
T. Born: Amgen employee and stockholder
P. Kaur: Amgen employee and stockholder

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### P0860 PHARMACOECONOMIC ANALYSIS OF BIOSIMILAR INFLIXIMAB (CT-P13) IN FIVE EUROPEAN COUNTRIES IN 2015


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**Introduction:** Biosimilar infliximab (CT-P13) was recently approved by the US Food and Drug Administration in April 2016, following its approval by the European Medicines Agency in 2013. Due to its lower price compared with the infliximab reference product (RP), it is possible that use of biosimilar infliximab could offer a method to reduce the economic burden associated with biologic therapy and increase the number of patients accessing treatment.

**Aims & Methods:** This study aimed to analyse the real-world pharmacoeconomic effects of biosimilar infliximab use in Europe in 2015. To evaluate market share for biosimilar infliximab, surveys were conducted by IMS Health in France, Germany, Spain, UK and Italy (with market share defined as the number of vials of biosimilar infliximab sold, expressed as a percentage of the number of RP vials sold). To evaluate costs, public prices for biosimilar infliximab and RP in France, Spain, UK and Italy were used; prices in Germany were calculated according to IMS Health sales data.

**Results:** In the first quarter of 2015, market share of biosimilar infliximab in France, Germany, Spain, UK and Italy was 0, 2.0, 4.4, 0.1 and 0.3%, respectively (Table 1). Market share in the fourth quarter was 10.7, 17.2, 22.7, 25.3 and 28.8%. For 2015, total cost savings associated with biosimilar infliximab use in Germany, Spain, UK and Italy were €1,354,954, 5,974,960, 2,311,602 and 3,793,025, respectively. There were no cost savings in France as public prices for biosimilar infliximab and RP were the same. With the cost savings calculated, it was estimated that use of biosimilar infliximab instead of RP could allow up to 1,085 extra patients in Spain per year to access biologic therapy.

**Conclusion:** This study has shown the real-world cost savings that were associated with use of biosimilar infliximab in five European countries in 2015. Due to its cost competitiveness, biosimilar infliximab has rapidly entered into use, while the market share of RP has decreased. Even though the price of biosimilar infliximab and RP are the same in France, use of biosimilar infliximab has grown gradually in that country. Competition between the two products may drive down costs of both biosimilar infliximab and RP. As the market share of biosimilar infliximab increases, the economic burden in each country is expected to reduce, allowing more patients to access biologic therapy.

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S. Yoon: No funding was provided and the author has no conflicts of interest in this study. The author is a full-time employee of Celltrion.

### P0861 PREDICTORS OF LOSS OF RESPONSE TO ADALIMUMAB THERAPY; THE IMPORTANCE OF THERAPEUTIC DRUG MONITORING IN INFLAMMATORY BOWEL DISEASES


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**Introduction:** Therapeutic drug monitoring (TDM) measuring drug trough levels (TL) and antidrug antibodies (ADA) may aid the therapeutic decision in patients with inflammatory bowel disease (IBD) who loose response to anti-TNF therapy.

**Aims & Methods:** Our aim was to evaluate the frequency and predictive factors of loss of response to adalimumab therapy and the role of the therapeutic drug monitoring to predict the loss of response in adalimumab treated IBD patients. 74 IBD patients (with 94 TDM measurements, CD/UC 59/15, male/female 32/42, mean age CD/UC: 38/31 years, mean duration of adalimumab therapy CD/UC: 147.6/43.7 weeks) were enrolled in this consecutive cohort from two referral IBD centres in Hungary. Demographic data were comprehensively collected and a harmonized monitoring strategy was applied. Previous and current therapy, laboratory data and clinical activity at the time of the TL and ADA measurement were recorded. Patients were evaluated either at the time of suspected LOR or during follow-up. TDM measurements were done by commercial ELISA (LISA TRACKER, Theradiag, France).

**Results:** Among 74 IBD patients, the probability of ADA positivity and low TL ($<4.5\ \mu g/mL$) was 8.1% and 13.8% in the first year and 11.4% and 28.8% and in the second year after start of adalimumab therapy in Kaplan-Meier analysis. The frequency of previous and current steroid and azathioprine exposure were 95.9%/29.7% and 73.3%/53.3% and previous anti-TNF therapy was present in 74% (in CD 69%, in UC 93.3%) in the IBD cohort. Dose intensification was needed in 38.7% during the study period. The combination of normal TL and no ADA, normal TL and high ADA, low TL and no ADA and low TL and high ADA were observed in 63.5%, 6.8%, 23% and 6.8% at TDM measurement. Predictors of the dose intensification were female gender ($p = 0.06$, HR: 2.1), concomitant steroid therapy ($p = 0.01$, HR: 2.57) and ADA positivity ($p = 0.005$, HR: 3.26) with Cox-regression model ($p < 0.05$). Predictors of loss of response were female gender ($p = 0.004$, HR: 4.9), dose intensification ($p = 0.009$, HR: 3.75) and there was a positive trend for concomitant steroid therapy ($p = 0.06$, HR: 2.71) and previous anti-TNF therapy ($p = 0.15$, HR: 2.39). Predictors remained unchanged if the 94 TDM episodes were analysed separately.

**Conclusion:** Our results suggest that ADA development, low TL and need for dose intensification are frequent during adalimumab therapy and support the use of routine TDM assessment in IBD patients. Female gender, concomitant steroid therapy and ADA positivity were predictors of dose intensification and female gender and dose intensification predicted loss of response.

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### P0862 EFFICACY AND SAFETY OF VEDOLIZUMAB FOR INDUCTION OF REMISSION IN INFLAMMATORY BOWEL DISEASE- THE ISRAELI EXPERIENCE


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**Table 1:** Percentage of VDZ Patients (UC and CD) With Mucosal Healing

| Indication | Ref. | N | Assessment Method | Assessment Time Point | % of Patients With Mucosal Healing |
|---|---|---|---|---|---|
| UC | 1 | 59 | Mayo endoscopic score: 0 or 1 | Week 30 | 72% |
| | 2 | 29 | Colonoscopic evaluations | Median: 22 weeks (range 9–47 weeks) | 69% |
| | 3 | NR | Mayo endoscopic score: 0 or 1 | NR | 66% |
| | 4 | 14 | Mayo endoscopic score: 0 or 1 | NR | 57% |
| CD | 2 | 22 | Colonoscopic evaluations | Median: 22 weeks (range 12–52 weeks) | 30% |
| | 1 | 82 | Healing of all ulcers and/or erosions | Week 30 | 21% |
| | 3 | NR | Healing of all ulcers and/or erosions | NR | 20% |
| | 4 | 23 | CDEIS score: $<3$ | NR | 17% |

NR: Not Reported; CDEIS: Crohn's disease endoscopic index of severity.

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**Introduction:** Vedolizumab (VDZ) is an effective agent recently approved by both FDA and EMA for the treatment of ulcerative colitis (UC) and Crohn's disease (CD).

**Aims & Methods:** The aim of this study was to describe our real-life experience with VDZ in a large national cohort of patients with inflammatory bowel diseases (IBD), and specifically, to assess its efficacy for induction of clinical remission, steroid-free clinical remission and discontinuation of systemic corticosteroids by week 14.

**Methods:** Patients with IBD and treated with VDZ were prospectively enrolled. Those receiving$\geq$ 4 infusions (week 0, 2, 6,14) were included, as well as patients discontinuing VDZ earlier due to primary non-response or adverse effects (AE). Clinical, laboratory and endoscopic data were collected. Clinical remission was defined as Harvey Bradshaw index (HBI) $<5$ for CD, partial Mayo score $<2$ or Simple Clinical Colitis Activity Index (SCCAI)$<4$ for UC; physician's global assessment (PGA) was used when clinical scores were unavailable.

**Results:** A total of 166 patients receiving VDZ between January and November 2015 were included; after exclusion of patients that did not complete the induction protocol or did not have sufficient clinical data, 110 patients (CD-67,UC −35; unspecified IBD (IBD-U) – 4, pouchitis −2, ileostomy-2) were retained for analysis; For CD, the mean age at treatment onset was $39.6 \pm 17.7$ years, and mean disease duration was $12.8 \pm 9.4$ years. For UC and IBD-U, the mean age at treatment onset was $34.3 \pm 44$ years, and mean disease duration was $8.0 \pm 31$ years. Most patients (95.4%) failed at least one previous biologic therapy. For CD, clinical remission was achieved in 25/67 (37%) and steroid-free remission in 18/67 (26.5%) of the patients by week 14; 10/19 (52.6%) of the patients receiving systemic corticosteroids at onset of VDZ therapy discontinued steroids. VDZ was discontinued by 16/67 (23.8%) before week 14 due to primary non-response. Fifteen patients (22.4%) were hospitalized during VDZ treatment and 9/67 (13.4%) required surgery. For UC and IBD-U (combined), clinical remission was achieved in 14/39 (35.3%) and steroid-free remission in 9/39 (23%) of the patients by week 14; 9/18 (50%) of the patients discontinued systemic steroids. VDZ was discontinued for primary non-response in 9/39 (23%) of the patients. Seven (17.9%) patients were hospitalized and 5/39 (12.8%) were referred for colectomy. The main AEs observed included CMV Colitis, *Clostridium difficile* and campylobacter infection [1/110 (0.8%) patients each], transient hearing loss, skin rashes and fever within 24 hours of VDZ infusion [2/110 (1.6%) patients each].

**Conclusion:** In a large cohort of IBD patients with refractory disease, VDZ was effective in induction of clinical remission and steroid-free clinical remission. Treatment had a favorable safety profile. Thus, in accordance with recently published data, VDZ is an effective real-life therapy for IBD.

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## P0863 SYSTEMATIC LITERATURE REVIEW OF REAL-WORLD EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB IN ADULT ULCERATIVE COLITIS AND CROHN'S DISEASE PATIENTS

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**Introduction:** Vedolizumab (VDZ), a gut-selective monoclonal anti-integrin antibody, is approved for the treatment of moderate-to-severely active Crohn's disease (CD) and ulcerative colitis (UC) in adults.

**Aims & Methods:** This study aimed to provide a systematic summary of recently published reports describing real-world effectiveness and safety of VDZ to date. MEDLINE-, Cochrane- and Embase-indexed publications and conference abstracts (n $\geq$10) were searched from 1 January 2014 to 1st April 2016, to identify studies reporting VDZ outcomes. Reports for patients $<18$ years of age or on off-label VDZ use were excluded.

**Results:** 51 reports were identified (4 manuscripts and 47 conference abstracts) describing a total of 5,775 VDZ patients. The majority of VDZ-treated patients had prior exposure to $\geq$1 anti-tumour necrosis factor (TNF) therapy; definitions of clinical remission differed between studies (partial Mayo score, simple clinical colitis activity index, Harvey-Bradshaw index, Crohn's disease activity index, clinician assessment). In UC, real-world clinical remission rates at week 14 ranged from 24–55% (6 studies). Three UC VDZ studies reported steroid-free clinical remission rates at week 14 ranging from 19%–36%. In 2 UC studies not reporting clinical remission rates, marked reductions in disease activity scores (DAIs) from baseline at week 14 were observed. Mucosal healing was observed in 57–72% of patients in 4 UC studies (Table 1). In CD, real-world clinical remission rates at week 14 ranged from 14–38% (7 studies). Three CD studies reported steroid-free clinical remission rates between 19%–31% at week 14. In 3 CD studies not reporting clinical remission rates, marked reductions in DAIs from baseline at week 14 were observed. Mucosal healing was observed in 17–30% of patients in 4 CD studies (Table 1). VDZ patients experiencing adverse events (AEs) ranged from 4–42% (13 studies); rates of infection ranged from 4–13% (7 studies). One study reported serious AEs in 8% of VDZ patients (2% of VDZ patients experienced a serious infection).

**Conclusion:** Real-world clinical effectiveness and safety data for VDZ confirm benefit for moderate-to-severely active UC and CD in largely anti-TNF-refractory populations. Evidence from larger VDZ cohorts over longer periods are required to support these findings and support the efficacy and safety outcomes in subpopulations of patients, including those naive to biologic therapy already demonstrated in the GEMINI studies.

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A. Solaman: AS is an employee of a research agency commissioned by Takeda Development Centre Europe Ltd. to conduct the study.
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## P0864 NO DIFFERENCE IN IMMUNOGENICITY OF THE ORIGINAL AND BIOSIMILAR INFLIXIMAB IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Infliximab (IFX) is a source of potential immunogenicity for patients, with the occurrence of anti-infliximab antibodies (ATI) and different autoantibodies such as antinuclear (ANA), anti-double-stranded DNA (anti-dsDNA), or anti-extractable nuclear antigens (anti-ENA) antibodies. Recently introduced biosimilar IFX seems to be identical to the original drug from the clinical and pharmacological points of view. However, even minor modification of molecular structure could potentially alter the immunogenicity of the drug.
**Aims & Methods:** To compare the incidence of immunogenicity of IFX in patients treated by biosimilar and original preparation. Sera from 60 previously IFX-naive patients treated by the biosimilar IFX (Remsima$^{TM}$) and 71 patients treated by the original preparation (Remicade®) were analyzed at treatment weeks 2 and 14 (W2 and W14) on ATI, ANA, anti-dsDNA and anti-ENA antibodies. ATI were detected by ELISA (Shikari, Matriks Biotek, Turkey). ANA and anti-dsDNA were detected by indirect immunofluorescence (ImmunoConcepts, USA and Orgentec, Germany, respectively), anti-ENA antibodies were analyzed by ELISA (Immco, USA). A chi-square statistic was used to investigate whether distributions of measured qualitative variables differ between two groups. P-values $< 0.05$ were considered significant.
**Results:** No significant difference in proportion of patients with positive ATI and ANA were observed at W2 between original and biosimilar IFX. None of patients was positive for anti-dsDNA and anti-ENA at W2. Similarly, at W14 the proportion of patients with positive anti-bodies (ATI, ANA, anti-dsDNA and anti-ENA) was not different comparing therapy with original and biosimilar IFX (Table 1).

**Table 1.**

| | | ATI | ANA | ANA in high titre (≥1:640) | Anti-dsDNA | Anti-ENA |
|---|---|---|---|---|---|---|
| | Biosimilar IFX | 3% | 18% | 2% | 0% | 0% |
| **W2** | Original IFX | 10% | 14% | 3% | 0% | 0% |
| | p-value | ns | ns | ns | ns | ns |
| | Biosimilar IFX | 7% | 30% | 18% | 3% | 2% |
| **W14** | Original IFX | 11% | 38% | 17% | 3% | 3% |
| | p-value | ns | ns | ns | ns | ns |

**Conclusion:** Original and biosimilar IFX have comparable immunogenicity in patients with inflammatory bowel disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0865 RISK FACTORS ASSOCIATED WITH THE NEGATIVIZATION OF ANTI-HBS ANTIBODIES IN INFLAMMATORY BOWEL DISEASE PATIENTS

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**Introduction:** The vaccine against hepatitis B (HBV) is less effective in patients with inflammatory bowel disease (IBD) than in the healthy population. Furthermore, it has been suggested that anti-HBs antibodies negativization rate following a successful vaccination is higher in such patients compared with healthy controls. The aim of this study was therefore to evaluate the anti-HBs negativization rate in a cohort of IBD patients and to investigate the risk factors associated to such loss.
**Aims & Methods:** Inclusion criteria: IBD patients not infected by HBV who were successfully vaccinated (determined as titres of anti-HBs $>10$ IU/L following vaccination) between 2008 and 2010. Follow-up period: from the date of vaccination until 2016. Procedures: Anti-HBs titres were retrospectively collected from the clinical history of the patients. Events were considered as negativization if antibodies titres were $<10$ IU/L at any serology. Statistical analysis: Logistic regression was applied, being the dependent variable the negativization of anti-HBs, and possible risk factors were investigated as covariates (type of IBD, gender, smoking habit, age of the patients at vaccination, anti-HBs titres after vaccination, and treatment with immunosuppressants or biologics).
**Results:** 95 patients were included (65% Crohn's disease, 52% female, 26% smokers, median of the age at vaccination: 38 years). During vaccination, 24% of patients were treated with immunosuppressants and 15% with biologics. Median follow-up was 23 months (range: 4–135 months) and the prevalence of negativization was 25%. The proportion of patients who lost antibody titles was significantly higher among those who had anti-HBs $<100$ IU/L (measured at 1–6 months after vaccination) compared to those with anti-HBs $>100$ IU/L (78% vs. 22%; $p < 0.01$). The predictive model of developed negativization (shown in the table) corroborated that titles of anti-HBs $>100$ IU/L were associated with a reduced probability of negativization, while treatment with biologics during vaccination markedly increased the risk of losing anti-HBs.

| | B | S.E. | p value | OR | 95% C.I.for OR |
|---|---|---|---|---|---|
| Anti- HBs $>100$ IU/L | −2.8 | 0.9 | $<0.01$ | 0.06 | 0.01–0.36 |
| Biologics | 1.6 | 0.7 | 0.02 | 5.16 | 1.2–21.18 |

**Conclusion:** Negativization of anti-HBs antibodies in IBD patients is much more common in patients with low post-vaccine antibody titres and in those treated with biologics during vaccination.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0866 AZATHIOPRINE IN THE MAINTAINANCE OF STEROID-FREE REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS: EFFICACY AND SAFETY IN FIVE YEARS OF FOLLOW-UP

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**Introduction:** Purine analogue azathioprine (AZA) is widely used for induction and maintenance of remission in steroid dependent patients with inflammatory bowel disease (IBD). The treatment must be withdrawn in 5–30% of patients due to the occurrence of adverse events.
**Aims & Methods:** We investigated its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients three year after the institution of treatment. Data from consecutive IBD outpatients referred in our Institution, between 1985–2014, 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 2684 consecutive IBD outpatients visited in the index period, AZA was prescribed to 398 patients, 216 (54.3%) were affected by Crohn's disease (CD) and 182 (45.7%) by ulcerative colitis (UC). One hundred and thirty-eight patients with a follow-up $<60$ months were excluded from the study. Two hundred and sixty patients were evaluated, 145 (55.8%) with CD and 115 (44.2%) with UC. One hundred and forty-six (56.2%) were male and 114 (43.8%) female (average age of $34.85 \pm 14.92$ SD years, range 14–74 y.). Five year after the institution of treatment, 135 (51.9%) patients still were in steroid-free remission (86 CD vs 49 UC, 59.3% and 42.6%, respectively, $p = 0.0087$), 71 (27.3%) had a relapse requiring retreatment with steroids (29 CD vs 42 UC, 20% and 36.5%, respectively, $p = 0.0033$), 54 (20.8%) discontinued the treatment due to side effects (30 CD vs 24 UC, 20.7% and 20.9%, respectively). Loss of response from 1$^{st}$ to 5$^{rd}$ year of follow-up was low, about 18%.
**Conclusion:** Five years after the onset of treatment 52% of patients did not require further steroid courses. After the first year loss of response was low in four 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 of Interest:** All authors have declared no conflicts of interest.

## P0867 IS FECAL CALPROTECTIN THE BETTER TOOL TO MONITOR DISEASE ACTIVITY IN PREGNANT IBD PATIENTS?

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**Introduction:** Active inflammatory bowel disease (IBD) increases the risk of adverse pregnancy outcomes, and maintaining clinical remission during pregnancy is of pivotal importance. It is difficult to validate IBD activity indexes in pregnant women because several parameters are affected by and change throughout pregnancy, e.g. laboratory markers, nausea, and stool frequency. Levels of fecal calprotectin (FC) greater than 100 microgram/gram have been found to predict Crohn's disease activity with greater accuracy than C-reactive protein (CRP) among non-pregnant patients.[1]Few, if any, studies have examined FC in pregnant IBD women as a marker for disease activity.

**Aims & Methods:** Pregnant women with IBD who received treatment with anti-TNF-alpha were prospectively recruited from seven tertiary hospitals in Denmark and Australia. Disease activity was assessed prospectively by a physician global assessment (PGA) as active or in remission in the 6 months pre-conception period, in each trimester and the first 6 months post-partum. We investigated if FC levels greater than 100 microgram/gram and/or CRP greater than 10 mg/L correlated with PGA of disease activity in the pre-conception period, in each trimester of pregnancy and/or postpartum. Demographics, disease activity and medication were prospectively documented. Blood and stool samples were obtained to determine CRP and FC, respectively. Pearson's chi-squared test was applied for comparison.
**Results:** Of the 42 pregnant IBD patients recruited, 33 (79%) had Crohn's disease and nine (21%) had ulcerative colitis. A total of 161 fecal samples and 192 blood samples were collected during the five periods of investigation. Disease activity was observed in the pre-conception period in 17 (40%); 1st trimester, 13 (31%); 2nd trimester 15 (36%); 3rd trimester, 17 (40%); and postpartum, 17 (40%). FC was significantly correlated with disease activity at all five periods of investigation ($p < 0.001$). In contrast, CRP was not correlated with disease activity at any time point ($p > 0.05$) apart from 2nd trimester ($p = 0.01$).
**Conclusion:** Our data suggest that FC is superior to CRP as a monitoring tool for disease activity during pregnancy among women with IBD. FC testing can be performed noninvasively and easily which is of great importance during pregnancy. These data should assist clinicians in the management of pregnant IBD patients.
**Disclosure of Interest:** M. Julsgaard: MJ has served as a speaker, compensated by MSD, Ferring, UCB, and Takeda.
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C.L. Hvas: CLH has served as a speaker, compensated by AbbVie, MSD, Takeda, Tillotts.
J. Fallingborg: JF has been on the advisory board for AbbVie and MSD. He has received research grants for other investigator-driven studies from Abbvie and Ferring.
J. Kjeldsen: JK has served as a speaker, compensated by MSD, Bristol-Myers Squibb, and Takeda.
M.P. Sparrow: MPS has received speaker fees from AbbVie, Ferring, Hospira, Janssen, Shire and is on the advisory boards for Hospira, Janssen, and Takeda.
S. Wildt: SW has served as a speaker compensated by MSD and Takeda, and is on the advisory boards for Tillotts and MSD.
S. Bell: SJB has received speaking honoraria from and acted as a consultant for Abbvie and Janssen. She has received research grants for other investigator-driven studies from Abbvie, Janssen, and Shire, Australia.
All other authors have declared no conflicts of interest.

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### P0868 OPEN LABEL OBSERVATIONAL STUDY EVALUATING THE EFFECT OF INDUCTION THERAPY WITH VEDOLIZUMAB IN PATIENTS WITH MODERATE TO SEVERE INFLAMMATORY BOWEL DISEASE INTOLERANT/RESISTANT TO AT LEAST TWO BIOLOGICALS

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**Introduction:** Vedolizumab is a fully humanized monoclonal IgG1 antibody targeting $\alpha 4\beta 7$ integrin that has shown its efficacy in patients with inflammatory bowel disease (IBD) even after failure of anti-TNF therapy. However, its effect as a third line therapy in real-life circumstances remains to be established.
**Aims & Methods:** In this prospective, multicentric, observational cohort study we aimed to evaluate the effects of vedolizumab induction therapy in a real-life setting. 150 consecutive adult IBD patients with moderate to severe disease and known primary or secondary failure/intolerance to at least two biologicals were included in a compassionate early access program. Vedolizumab (300 mg intravenously) was administrated at weeks 0, 2, 6 and optionally at week 10 for Crohn's Disease (CD) patients. Efficacy was evaluated by physician's assessment at week 10 for Ulcerative Colitis (UC) and week 14 for CD. In case of response, maintenance therapy was started. Remission was defined based on Harvey-Bradshaw index (HBI) or CDAI for CD patients and total Mayo score for UC patients.
**Results:** In this study, data from 121 patients (80.6%; mean age $40.7 \pm 13.4$ y; mean disease duration $13.3 \pm 8.7$ y; 54% concomittant oral steroids at week 0) are presented of which 79 patients had CD (62.3% female; mean HBI 15.7, mean CDAI 306.9) and 42 patients were known with UC (41.5% female; mean total Mayo 9.6). Based on physician's assessment at week 10 for UC and week 14 for CD, we report a clinical response in 62/79 or 78.5% of patients with CD and 31/42 or 73.8% of patients with UC with no difference between steroid users and non-users (73.1% clinical response in concomittant steroid use versus 80% in steroid free patients). Clinical remission was found in 34.2% of CD patients (defined as CDAI $\leq 150$ or HBI $\leq 4$) but in only 5.9% of UC patients (Mayo score $\leq 2$). Clinical response according to changes in disease activity score was found in 68% of UC patients (defined as a drop in Mayo score with 3 points and at least 30% from baseline) and 69.7% CD patients (CDAI drop $> 100$ or HBI $>/= 3$). No deaths were reported during the course of this study. Nine patients needed colectomy because of non-response ($n = 6$), acute subobstruction ($n = 1$) or perforation during colonoscopy ($n = 1$). In one patient ileostomy and drainage of a perirectal abscess was required.
**Conclusion:** In this retrospective cohort study studying the real life effects of third line administration of vedolizumab in IBD patients intolerant/resistant to at least two biologicals, approximately 70% achieved a clinical response after 10 to 14 weeks.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0869 ULCERATIVE COLITIS: DISEASE COURSE AND PROGNOSIS DURING THE FIRST YEAR OF DISEASE

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**Introduction:** Ulcerative Colitis (UC) is a chronic immune-mediated disease affecting the colon and rectum. While the majority of patients will present a mild and moderate disease, approximately 15% will require hospitalization and 5% will be refractory to conventional management and potentially require surgery.
**Aims & Methods:** We sought to evaluate the clinical course of patients with UC during the first year of diagnosis and determine potential predictors of the need of anti-TNF therapy and surgery. This was a single-center, retrospective study including patients with an established diagnosis of UC. Demographic and clinical data were retrieved from patient's medical charts. Logistic regression analysis were performed in order to evaluate potential predictors of the need for surgery or biologic therapy.
**Results:** 395 patients with UC were included in this study. Patient's characteristics are presented in Table 1. In the first year following diagnosis, 336 (85.1%) required therapy with aminosalycilates, 202 (51.1%) steroids and 48 (12.2%) with thiopurines. Ten patients (2.5%) required biologic therapy and 9 patients (2.3%) underwent surgery. During the first year of disease, 47 patients (11.4%) developed an episode of severe acute colitis (SAC). Colectomy was more common amongst this group (OR 35.4 IC95% [11.0–114.8], $p < 0.001$). In regression analysis, extensive disease was the only independent predictor of requiring anti-TNF therapy (OR 3.813 IC95%[1.194–12.172], $p = 0.024$) and surgery IC95%(OR 8.353 [1.131–61.671], $p = 0.037$).
**Conclusion:** A subgroup of patients with UC present with an early aggressive severe course. The extension of inflamed bowel and developing an episode of ASC represent important prognostic factors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0870 THE INCIDENCE OF SUBOPTIMAL THERAPY AFTER INITIATING A SECOND TUMOUR NECROSIS FACTOR ANTAGONIST IN PATIENTS WITH ULCERATIVE COLITIS: A MULTI-COUNTRY CHART REVIEW

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**Introduction:** Patients with ulcerative colitis (UC) treated with tumour necrosis factor antagonists (anti-TNF) may require treatment modifications (i.e., dose

escalation, switch to another anti-TNF, surgery, or addition of other medications). Such changes can be used as surrogate of loss of response and may be considered as indicators of suboptimal therapy.
**Aims & Methods:** Our aim was to quantify the incidence of suboptimal therapy among adult patients with UC treated with a second anti-TNF using data from real-world clinical practices. A retrospective chart review study conducted in six countries (Canada, France, Germany, Italy, UK, and Spain) recruited UC patients initiating anti-TNF therapy between June 2009–2013. We measured the incidence of suboptimal therapy over two years and time to the first indicator of suboptimal therapy among patients who switched from initial anti-TNF to a second anti-TNF. Indicators of suboptimal therapy with a second anti-TNF included anti-TNF dose escalation (assessed >4 months after index to allow for initial dose optimization), augmentation with aminosalicylates, immunomodulators, or corticosteroids, discontinuation of anti-TNF therapy, switching to another anti-TNF, and UC-related surgery. Time to the first occurrence of the indicator of suboptimal therapy was measured using the Kaplan-Meier Method, where patients were censored after discontinuation of therapy or at the end of the follow-up period.
**Results:** The study included a total of 538 UC anti-TNF naïve patients of which 111 (20.6%) patients had initiated a second anti-TNF [mean age (SD): 40.7 (14.9) years, 45% female]. Median duration with the first anti-TNF therapy was 9.8 months. 73.8% of patients had reported moderate to severe UC with a median duration of UC of 5.2 years. The majority of patients had left-sided or distal UC and pancolitis (35.1% and 50.0%, respectively). At the time of initiation of the second anti-TNF therapy, 69.4% of patients had an ongoing treatment with at least one non-biologic therapy. The proportion of patients on adalimumab, infliximab and golimumab as a second anti-TNF were 83.8%, 9.0%, and 7.2%, respectively. Within two years after initiating a second anti-TNF therapy, 51.4% patients had at least one indicator of suboptimal therapy. Discontinuation (27.9%) and dose escalation (17.1%) were the most frequent indicators of suboptimal therapy. Median time to at least one of the indicators of suboptimal therapy was 14.3 months (95% CI: 9.0 – 25.0).
**Conclusion:** Over half of UC patients treated with a second anti-TNF therapy experienced at least one indicator of suboptimal therapy within 2 years of therapy. The most common indicators were dose escalation and discontinuation with anti-TNF therapies. Future research should determine the potential for alternative therapies to improve treatment response rates among patients who experience loss of response with anti-TNF therapies.
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## P0871 PROBIOTICS ARE LESS EFFECTIVE THAN MESALAZINE IN MAINTAINING REMISSIONS IN IBD

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**Introduction:** The role of gut microbiota has become more appreciated in recent years emphasizing the IBD etiology. Probiotics are widely discussed for IBD and thought to work by altering the composition of the intestinal microbiota, the epithelial barrier function of the intestine, and have important immunoregulatory activity. Expanding this idea, probiotics have been subject for intensive research, mainly focusing on bifidobacteria and lactobacteria. However, existing reports of probiotic use in IBD are contradictory and even confusing.
**Aims & Methods:** The aim of this study is to compare therapeutic efficacy of standard treatment with mesalazine and novel probiotic strains with potent immunological features. Ninety-eight patients (34 CD, 64 UC) participate in the study. Colonic resistance studied in mucosal bioptates. Specially designed (T73) strain of P. Shermani with high antagonistic/immunoregulatory potential was orally given triple daily in a form of suspension containing $10^{12}$–$10^{14}$ bacteria/day. Patients without probiotic treatment formed second group (57.14%), they received mesalazine 1500 mg ($3 \times 500$ mg) daily as a basis therapy. Study duration was 50 weeks, treatment efficacy evaluated according to WGO, ECCO Guidelines and patients were assessed by clinical and endoscopic activity indices as well as by biopsies. The primary endpoint of the study was to compare efficacy in prevention of relapses.
**Results:** Systemic oral probiotic use significantly improved colonic resistance. There were relapses in 16 of 56 (28.57%) patients in second group (with mesalazine) and in 19 of 42 (45.24%) in probiotic group ($p = 0.007$). No statistically significant variations between UC and CD patients inside groups were found. CDAI score at the end of study was $12.37 \pm 5.14$ points lower in mesalazine group ($p > 0.05$). Abdominal pain, stool, and drug use for symptomatic therapies improved in both groups, too. Endoscopic picture and biopsies presented no specific differences between groups after study. Safety profiles and tolerability were satisfactory for both groups and without significant differences.
**Conclusion:** Probiotics are living microorganisms that exert health effects on the host; their use in IBD is promising. Our study shows that probiotic treatment of IBD patients with P. Shermani is safe but lacks efficacy in maintaining remission equivalent to the gold standard in IBD treatment – mesalazine. However, this study has limitations in both volume and control. Further controlled trials are needed to clarify whether probiotics alone are sufficient enough to prevent IBD relapses. At that point use of probiotics may have good potential when applied as an addition to mesalazine, acting on different mechanisms of IBD pathogenesis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0872 BIOSIMILAR INFLIXIMAB IS EFFECTIVE AND SAFE IN INFLAMMATORY BOWEL DISEASE PATIENTS NAIVE TO ANTI-TNF THERAPY: A TERTIARY CENTER EXPERIENCE

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**Introduction:** Biosimilar infliximab (IFX) has been approved in European Union for treatment of inflammatory bowel disease (IBD) since September 2013. The approval process included the extrapolation of clinical data from other indications, namely rheumatoid arthritis and ankylosing spondylitis. The data from clinical practice are therefore desirable to confirm the efficacy and safety of biosimilar IFX in IBD population.
**Aims & Methods:** The aim was to evaluate efficacy and safety of biosimilar IFX in patients with Crohn's disease (CD) and ulcerative colitis (UC) naïve to anti-TNF therapy. Data from consecutive patients with CD and UC starting on biosimilar IFX since January 2015 at our center were analyzed. Patients were assessed as non-responders (NR), partial responders (PR), or complete responders (CR) based on clinical, endoscopic, and laboratory parameters. Besides clinical and endoscopic evaluation, C-reactive protein (CRP) levels, faecal calprotectin (FC), blood count, IFX trough levels (TL), and antibodies-to-infliximab (ATI) were measured. All adverse events were also recorded. Final analysis was performed at week 38 (W38).
**Results:** One hundred and nineteen IBD patients (CD, 90; UC, 29, female 55.5%) were included into this analysis. The mean disease duration at anti-TNF therapy start was 6.2(±6.3) years. Thirty seven percent of patients had history of extra-intestinal manifestations, 27.7% were treated surgically in past, and 31.1% of CD patients had a history of perianal disease. By week 38, 84.1% of CD, and 65.2% of UC patients were assessed as CR or PR. Perianal disease was improved in 88% of patients. Among UC patients, one half of them achieved mucosal healing (Mayo endoscopic subscore 0 or 1) by W38. Therapy was intensified in11.9% of CD and 23.5% of UC patients. The mean IFX trough level at W38 was $4.5 \pm 5.5 \mu$g/mL, and 10% were positive for ATI. Therapy with biosimilar IFX was discontinued in 7 CD (7.8%) and 6 (20.7%) patients. Observed adverse events included mainly skin lesions (16), joint pain (14) and infectious complications (14). Fife patients were hospitalized for disease exacerbation, and 7 underwent surgery.
**Conclusion:** Both efficacy and safety of biosimilar IFX in this cohort of anti-TNF naive IBD patients seems to be comparable to that observed previously with originator IFX.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0873 CORRELATION BETWEEN ENDOSCOPIC AND HISTOLOGICAL HEALING IN ADULTS WITH MODERATE TO SEVERE CROHN'S DISEASE: DATA FROM EXTEND

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**Introduction:** Clinical remission and endoscopic healing are regarded as important treatment targets for patients with Crohn's disease (CD), but do not take into account histopathological healing. Concordance between endoscopy and histology scores for patients with CD is not well known.

**Aims & Methods:** We assessed the agreement between complete endoscopic healing and histological healing at baseline (BL) and week 52 in the colon and ileum segments of patients with moderate to severe CD randomized in the EXTEND study (N = 129). Concordance of each of the Simple Endoscopic Score for CD (SES-CD) subscores (ulcer size, ulcerated surface, and affected surface) measured in pooled samples from 3 colon segments (sigmoid/left, transverse, right colon) or ileum with Colonic Global Histologic Disease Activity Scores (CGHAS) for the colon samples or with Ileal Global Histologic Disease Activity Scores (IGHAS) for the ileal samples was performed using kappa statistic. Complete endoscopic healing was defined as SES-CD ulcer size subscore = 0, ulcerated surface subscore = 0, and affected surface subscore = 0 in the colon segments or in ileum. The SES-CD subscores in each of the colon segments had to = 0 to qualify as complete endoscopic healing. Two biopsies from each ileocolonic segment were evaluated for 8 histological variables, including epithelial damage, architectural damage, mononuclear cells in lamina propria, neutrophils in epithelium, erosion or ulceration, granuloma, proportion of ≥6 biopsy samples that were affected. Individual variables were scored independently and summed up to create CGHAS/IGHAS scores ranging from 1 (least severe) to 16 (most severe)[1, 2]. Histologic healing was defined as CGHAS or IGHAS ≤2. Centrally read SES-CD and CGHAS/IGHAS were used and patients were analyzed regardless of randomized treatment, disease location, and whether they had ulcers at BL. Data are reported as-observed.

**Results:** Fair/moderate to high agreement was observed at BL and week 52 between SES-CD subscores (ulcer size, ulcerated surface or affected surface) and CGHAS (for colon segments)/ IGHAS (for ileum) scores (Table). At week 52, for patients with evaluable colonic biopsies, SES-CD subscores = 0 were observed in 68% (53/78, data as observed) of patients for ulcer size and ulcerated surface, and by 65% (51/78) for affected surface subscores. CGHAS≤2 in the colon was observed in 67% (52/78) of patients. Of the patients with SES-CD subscores = 0 for ulcer size or ulcerated surface in the colon, 83% (44/53) also had CGHAS ≤2; the corresponding value for patients with affected surface = 0 was 84% (43/51). Similarly, for patients with evaluable ileal biopsies, 68% (52/77) of patients had SES-CD subscore = 0 for the 3 subscores evaluated and 75% (58/77) had IGHAS≤2 at week 52. Of the patients with SES-CD subscores = 0 in the ileum, 96% (50/52) also had IGHAS≤2. Concordance between SES-CD components and IGHAS/CGHAS scores is shown in the Table.

**Conclusion:** A high degree of concordance between SES-CD subcores and IGHAS/CGHAS was observed at week 52, as the majority of patients with complete endoscopic healing (using a very stringent SES-CD definition) also had histological healing. There was a greater concordance in the ileum than in the colon.

**Table:** Degree of Agreement (kappa values) Between SES-CD Subscores and IGHAS/CGHAS at Baseline and Week 52

| | BL N = 121 | | | Week 52 N = 78 | | |
|---|---|---|---|---|---|---|
| | CGHAS > 2 | CGHAS≤2 | κ* | CGHAS > 2 | CGHAS≤2 | κ* |
| Ulcer size = 0 | | | | | | |
| No | 75 | 1 | 0.37 | 17 | 8 | 0.50 |
| Yes | 30 | 15 | | 9 | 44 | |
| Ulcerated surface = 0 | | | | | | |
| No | 75 | 1 | 0.37 | 17 | 8 | 0.50 |
| Yes | 30 | 15 | | 9 | 44 | |
| Affected surface = 0 | | | | | | |
| No | 77 | 1 | 0.39 | 18 | 9 | 0.51 |
| Yes | 28 | 15 | | 8 | 43 | |
| | BL N = 113 | | | Week 52 N = 77 | | |
| | IGHAS > 2 | IGHAS≤2 | κ* | IGHAS > 2 | IGHAS≤2 | κ* |
| Ulcer size = 0 | | | | | | |
| No | 50 | 10 | 0.55 | 17 | 8 | 0.68 |
| Yes | 15 | 38 | | 2 | 50 | |
| Ulcerated surface = 0 | | | | | | |
| No | 50 | 10 | 0.55 | 17 | 8 | 0.68 |
| Yes | 15 | 38 | | 2 | 50 | |
| Affected surface = 0 | | | | | | |
| No | 53 | 10 | 0.60 | 17 | 8 | 0.68 |
| Yes | 12 | 38 | | 2 | 50 | |

*P < 0.001 for all comparisons.

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## P0874 TUBERCULOSIS IN INFLAMMATORY BOWEL DISEASE PATIENTS UNDER TREATMENT WITH ANTI TNF ALFA AGENTS: A FREQUENT COMPLICATION DESPITE RIGOROUS SCREENING

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**Introduction:** Although screening strategies for tuberculosis (TB) are applied to all patients before starting biologic therapy with anti TNF alfa agents, the risk of TB reactivation/infection remains a problem, especially in countries with high prevalence of infection. Our objectives were to evaluate the frequency of latent TB before and of active TB during biological treatment in patients with inflammatory bowel diseases (IBD).

**Aims & Methods:** Patients with IBD and biological treatment from Fundeni Clinical Institute, Bucharest, Romania were evaluated retrospectively. Demographic data (sex, age, rural/urban residence, profession), diagnosis (type, extension, severity of bowel disease), the results of TB screening (PPD test, Quantiferon), treatment, were noted. Patients diagnosed with active TB were contacted by phone and time of onset, TB symptoms, treatment, laboratory and radiological tests were noted.

**Results:** 156 patients with Crohn's disease and 45 with ulcerative colitis, 104 men, with mean age 39.1 years were included in the study. 100 received Infliximab and 101 Adalimumab. 42 (20.89%) patients had latent TB at screening, before starting anti TNF therapy: 23 patients were Quantiferon positive, 9 both PPD test and Quantiferon positive, 4 only PPD test positive. All received prophylactic treatment with Hydrazide. Seven patients were diagnosed with active TB after a mean time of 13+/−0.3 month form the start of biologic therapy, 5 being in remission and 2 with mild flares of IBD at the time of TB diagnosis. One patient received concomitantly immunosuppression, one oral cortisone, the rest being on anti TNF monotherapy. All cases were pulmonary TB: 3 pleurisy, 3 pneumonic, one miliary. Only one patient had latent TB at screening. Two patients had TB contact. The symptom present in all patients was cough, 4 patients had dyspnea, 3 had fever, 2 nocturnal sweating. Quantiferon test was positive for all.

**Conclusion:** Although 1 of 5 patients with IBD and indication for biological treatment have latent TB, most of the cases with active TB were diagnosed in patients with negative TB screening. To avoid delays in diagnosis patient's training regarding the most frequent symptoms and Quantiferon test can help.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0875 ADHERENCE TO ULCERATIVE COLITIS MANAGEMENT GUIDELINES BY ITALIAN GASTROENTEROLOGISTS: A MULTICENTRE PROSPECTIVE OBSERVATIONAL AIGO STUDY

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**Introduction:** Several guidelines and consensus are available for the therapeutic management of patients with ulcerative colitis (UC). The application of such criteria in daily practice improves the quality of care and increases patient satisfaction, however only few studies have evaluated the use of evidence-based therapy by physicians in their clinical practice.
**Aims & Methods:** The aim was to assess the adherence to UC management guidelines by Italian gastroenterologists. A multicentre prospective observational study on the adherence to the guidelines in UC was conducted in 26 gastroenterology (GI) units across Italy. Consecutive outpatients with a flare of UC were enrolled in the study. A questionnaire was administered to the attending physicians consisting of two sections, the first included questions about the GI unit, personal experience in inflammatory bowel disease (IBD), number of IBD/UC patients followed by the unit, the second included questions on the extension and severity of UC, specific medical treatment undertaken and adherence to the guidelines.
**Results:** Most of the centres (73%) were provided with an IBD outpatient clinic and a GI ward, 61.5% of the attending physicians classified themselves as gastroenterologists specialized in IBD. Five hundred seventy-two patients (325 males) were enrolled by high (40.9%), medium (37.9%) and low (21.2%) IBD volume units, and included 41.2% extensive colitis (mild-moderate: 79.1%, severe: 19.9%), 48.3% left-sided colitis (mild-moderate: 88.0%, severe: 12.0%), 10.5% proctitis (mild-moderate: 93.3%, severe: 6.7%). Mean age of patients: 49.3 yrs (range 18–87), mean age at diagnosis 40 yrs (range 8–79). In 88.8% of flares the management was considered by the attending physicians based on guidelines regardless of the physician's experience in IBD. Physicians from high IBD volume units referred more to ECCO guidelines (89.3% vs 63%). Rectal 5-ASA in left-sided and extensive colitis was less prescripted in low IBD volume unit (55% vs 80%) and by less experienced physicians (53% vs 76%). Conversely, physicians with less experience prescribed more anti-TNF therapy for mild–moderate UC (27% vs 10%).
**Conclusion:** The adherence of Italian gastroenterologists to the guidelines for the management of UC is high. In clinical practice, the size of IBD unit and the physicians experience in IBD may affect the compliance with guidelines.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0876 SKIN SIDE-EFFECTS OF BIOLOGIC THERAPY AND SYSTEMIC DRUGS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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**Introduction:** Crohn's disease and ulcerative colitis count among inflammatory bowel diseases (IBD). Currently, biologic therapy is the most advanced and most effective anti-inflammatory strategy in IBD treatment. Most common side effects of the treatment include skin manifestations. According to some authors the prevalence reaches about 20% of patients undergoing biological treatment. The biologic therapy becomes increasingly frequent therapeutic option in patients with IBD and as a result skin complications occur more frequently.
**Aims & Methods:** To compare the incidence of skin reactions in patients with IBD treated with biologic therapy with the incidence in IBD patients with other systemic treatment. The study was performed between 2009 and 2015 and 221 subjects were enrolled. All patients involved in the project suffered from Crohn's disease or ulcerative colitis and exhibited a skin reaction during the treatment. 167 subjects treated with biological agents with skin reaction were enrolled as cases. 54 patients treated with other systemic drugs such as azathioprine, methotrexate, mesalazine, sulfasalazine, and corticosteroids were included in the control group.
**Results:** Atopic dermatitis was interestingly the most frequent dermatosis that we diagnosed in both groups. In the case of occurrence of psoriasis, palmoplantar pustulosis and bacterial skin infections, we noticed some differences between the group of patients treated by biologic agents and the group with other systemic drugs. These differences did not reach the level of statistical significance.

Skin side-effects of IBD treatment

| | Biologic therapy | Other immunosupressants |
|---|---|---|
| **Atopic dermatitis** | 76 | 20 |
| **Psoriasis** | 16 | 2 |
| **Pyodermia** | 12 | 1 |
| **Palmoplantar pustulosis** | 9 | 1 |
| **Total** | 167 | 54 |

**Conclusion:** In some skin reactions, discontinuation of biologic therapy is necessary, in other cases the therapy may continue but the cooperation with a dermatologist is needed. We would like to help gastroenterologists and dermatologists with the management and raise their awareness in terms of skin diseases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0877 SYNERGY RESEARCH: INVESTIGATING THE COMBINED ACTION OF CHAMOMILE, MYRRH AND COFFEE CHARCOAL ON CHEMOKINE RELEASE OF ACTIVATED HUMAN MACROPHAGES

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**Introduction:** The herbal medicinal product Myrrhinil-Intest®, a combination of myrrh (Commiphora molmol E.), chamomile flower (Matricaria recutita 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]. In vitro studies revealed, that chemokine signaling of human macrophages is influenced by the plant extracts as part of an anti-inflammatory strategy. However, the occurrence of synergistic effects remains unexplored.
**Aims & Methods:** The present study aims to investigate the combined effect of the plant extract on chemokine (CXCL13 release) from activated human macrophages. The single effect of myrrh (MY), chamomile flower (KA) and coffee charcoal extract (CC) on CXCL13 release from LPS (100 ng/ml)-stimulated human macrophages was investigated after 24 hours incubation time using an ELISA test system. The inhibitory effect was characterized by calculation of IC50 values. Budesonide served as positive control. To characterize the combined effect, IC50 values were used to prepare combinations of two plant extracts in different concentrations (0–100%) and proportions to each other (3:1; 1:1; 1:3). Interpretation of the data was based on isobologram analysis and calculation of a combination index (CI; $= IC50_{comb.}/IC50_{single}$).
**Results:** LPS-induced CXCL13 release from human macrophages was inhibited after treatment with MY ($IC50 = 19\,\mu g/ml$), KA ($IC50 = 82\,\mu g/ml$) and CC ($IC50 = 106\,\mu g/ml$) whereby the extent of inhibition was comparable to budesonide. All combinations of two plant extracts resulted in synergistic effects with varying magnitude (CI from 0.87 to 0.46). The combination of CC and KA (ratio of 1:1) exhibited the strongest synergistic effect ($CI = 0.46$). Increasing amounts of CC resulted in increased synergistic activity ($CI_{coffee\ charcoal/myrrh\ (1:3)} = 0.73$; $CI_{coffee\ charcoal/myrrh\ (1:1)} = 0.60$; $CI_{coffee\ charcoal/myrrh\ (3:1)} = 0.51$).
**Conclusion:** Synergistic effects between all plant components contribute to the anti-inflammatory activity of the herbal combination.
**Disclosure of Interest:** C. Vissiennon: Author Cica Vissiennon is employed by Repha GmbH Biologische Arzneimittel. Financial funding for the experiments has been provided by Repha GmbH Biologische Arzneimittel.
K. Goos: Co-Author Karl-Heinz Goos is shareholder of Repha GmbH Biologische Arzneimittel.
All other authors have declared no conflicts of interest.

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## P0878 EFFECT OF ADALIMUMAB ON PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS IN ITALIAN CLINICAL PRACTICE SETTING: RESULTS FROM INSPIRADA

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**Introduction:** Limited real-world data are available regarding the effects of adalimumab (ADA) on Italian patients with moderate to severe ulcerative colitis (UC).
**Aims & Methods:** INSPIRADA was a single-arm, multi-country, open-label study that evaluated the effect of ADA on patients with UC treated according to usual clinical practice. Adults with active moderate to severe UC who failed immunosuppressive therapies and experienced rectal bleeding within 7 days of baseline (BL) were enrolled. Prior use of anti-TNF was allowed. Patients received 160/80 mg ADA at Week 0/2 followed by 40 mg of ADA every other week at Week 4 to Week 26. Patients who did not respond to ADA by Week 8 (PGA score $\geq$2 and did not achieve Simple Clinical Colitis Activity Index [SCCAI] response, defined as a decrease of $\geq$2 points compared to BL) were to discontinue ADA. Patients who lost response at or after Week 8 could escalate to 40 mg ADA weekly. Clinical outcomes included SCCAI response and remission (defined as an SCCAI $\leq$2). HRQoL (EQ-5D-5 L and SIBDQ), treatment satisfaction with medication (TSQM), and work productivity and activity impairment (WPAI) were measured from BL to week 26. Change (defined as 6 mo after start

of ADA vs 6 mo before) in health care resource use was calculated. Data for the intent-to-treat population in Italy were analysed. Missing data were imputed using last observation carried forward.
**Results:** Data from 48 Italian patients (39.6% female, mean age 41.3 yrs) were analysed. Mean SCCAI at BL was 8.0. At week 2, 83.3% achieved SCCAI response and 31.3% achieved SCCAI remission. At week 8, 75.0% achieved SCCAI response, 43.8% were in remission and 37.5% had no blood in stool. At week 26, 66.7% achieved SCCAI response, 41.7% were in remission and 45.8% had no blood in stool. Significant improvements, as early as within 2 weeks, in SIBDQ (15.7 points, $p < .001$), EQ-5D-5 L (0.13 index score and 19.5 VAS points, both $p < .001$), all 4 WPAI domains (−23.6%, −27.1%, −32.7%, −26.2%, all $p < .001$), and 2 of 4 TSQM domains (21.9%, 23.3%, all $p < .001$) occurred from BL to week 26. Significant decreases in number of hospitalization (UC-related:−0.21; all-cause: −0.23, both $p < .05$), all-cause hospitalization length of stay (-2.19 days, $p < .05$), and UC-related outpatient visit (-2.0, $p < .001$) occurred in the 6 mo period after starting ADA compared to 6 mo before starting ADA. No new safety signals were identified from the evaluation of adverse events.
**Conclusion:** Real-world rates of response, remission and improvements in HRQoL with ADA for Italian patients with moderate to severe UC were clinically meaningful. ADA improved work productivity, increased patient satisfaction with therapy and reduced health care resource use for these patients.
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## P0879 ULCERATIVE COLITIS: ARE WE DEVALUING ITS PROGRESSIVE CHARACTER?

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**Introduction:** Ulcerative Colitis (UC) is a chronic disease but its progressive character, with structural damage is insufficiently studied.
**Aims & Methods:** To analyze a group of patients without bias referral, as the clinical course the morphological damage and functional status. We evaluated patients diagnosed with UC established between 01–01–2000 and 31–12–2004, residing in direct referral area of the hospital, having determined medication use, colectomy rate, structural damage (''lead pipe'', stenosis, pseudopolyp, fibrous bridges) or functional anorectal (Prospective evaluation with Cleavland Clinic Incontinence Score, CCIS and Fecal Incontinence Quality of Life, FIQL).
**Results:** We identified 104 patients, 47% female, mean age at diagnosis of $38 \pm 17$ years, 24% proctitis, left colitis 57%, 19% pancolitis. In 3 patients it has not been possible to obtain follow-up data. Of the studied patients, 56% were in need of corticosteroid therapy, 38% of immunosuppressants and 16% of anti-TNFs. After a mean follow-up of $13 \pm 2$ years, it was met structural damage in 25 patients (25%), protocolectomy in 5%, ''lead pipe'' in 15%, 16% pseudopolyp stenoses and 3% fibrous bridges. It was reference to anorectal disorders in 49% (mostly self-limited and previous episodes of incontinence) but including persistent incontinence in 10%. There was an increased incidence of structural damage and anorectal dysfunction in patients who needed corticosteroid therapy ($p = 0.001$), immunosuppressants ($p < 0.001$) and anti-TNF ($P = 0.002$) and a correlation between structural damage and anorectal dysfunction ($p < 0.05$). There is no correlation between age and anorectal dysfunction, including incontinence episodes.
**Conclusion:** CU is a disease with structural and functional consequences in a significant subset of patients. This should be incorporated in the definition of the therapeutic strategy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0880 SAFETY PROFILE OF ANTI-TNF ALPHA THERAPY IN THE ELDERLY – A COMPARATIVE STUDY

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**Introduction:** TNF alpha is a key cytokine in immune regulation and defense against infections and malignancies. The ageing process has been associated with immune system functional changes, which could increase susceptibility to adverse events (AE). Advanced age has been suggested as a risk factor for infectious complications among patients with Inflammatory Bowel Disease (IBD) treated with anti-TNF alpha agents; however, safety data regarding biological therapy in elderly patients with IBD is still limited.
**Aims & Methods:** The aim of this study was to evaluate the AE of elderly patients with IBD treated with an anti-TNF alpha agent. A retrospective analysis was conducted in all IBD patients $\geq$ 60 years old treated with Infliximab (Group A) between 2006 and 2014. A control group of patients with <30 years old (Group B) was randomly selected. The probability of a causal association between each AE and the drug was determined by using an imputability score based in chronologic and clinical criteria and then classified as ''not related'', ''doubtful'', ''possible'', ''likely'' or ''definite''.
**Results:** Twenty patients were included in each group. The mean age at the beginning of Infliximab therapy was of 63 and 21 years and the mean treatment time with the drug was of $39 \pm 29$ months (total of 482 infusions) and of $41 \pm 26$ months (total of 504 infusions) in group A and B, respectively. Patients in group A had more comorbidities, the most prevalent being hypertension (45%), dyslipidemia (20%) and diabetes (15%). An annual rate of 1.1 AE/patient (group A) and 1,0 AE/patient (group B) was recorded. In both groups, 10 patients had at least one infection and 4 patients had at least one infusion reaction. Serum sickness-like disease occurred in 6 patients of group A and in 1 patient of group B. Thirteen severe AE had an association that was at least possible with the drug: 8 in group A and 5 in group B. Mortality was null and only 1 event resulted in permanent disability and/or progressive disease.
**Conclusion:** In this series, the annual rate of AE related to anti-TNF alpha therapy was low in both groups. With the exception of serum sickness-like disease, which was more frequent among elderly patients, the range of events was similar. Although severe AE related to the drug were rare, their occurrence was higher in individuals with $\geq$ 60 years old.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0881 SAFETY AND EFFICACY OF FERINJECT® IN THE TREATMENT OF IBD-RELATED IRON DEFICIENCY ANAEMIA UNDER DAILY PRACTICE CONDITIONS – RESULTS FROM A NON-INTERVENTIONAL POST-MARKETING SURVEILLANCE STUDY IN GERMANY

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**Introduction:** Iron deficiency (ID) and iron deficiency anaemia are common complications in IBD patients with significant detrimental effects on Quality of Life. Anaemia in IBD is attributable to chronic blood loss and/or impairment of iron intake and absorption. International guidelines favour the use of intravenous (IV) iron supplementation in IBD patients, since oral supplements are frequently poorly tolerated and have been shown to exacerbate inflammation. Ferric carboxymaltose (FCM) is a recently-developed IV iron preparation that has been shown in clinical trials to be safe and effective. Ferinject® (FCM, 50 mg ferric iron(III)/ml suspension) allows application of single doses up to 1,000 mg per week, infused over 15 minutes.
**Aims & Methods:** For post-marketing surveillance (PMS), a prospective non-interventional study (NIS) was performed from Nov 2008 to Aug 2010, aiming to assess the efficacy of ferinject® in clinical practice in a large cohort of IBD patients. In addition, the study investigated the tolerability of ferinject® under routine conditions and the influence of rapid, high-dosed application on time and effort of physicians and patients. Primary endpoints were normalisation of Hb or increase of 2 g/dL, and normalisation of serum ferritin and transferrin

saturation (TSAT). AEs, clinical symptoms and disease activity indices (CD:CDAI/UC:CAI) were also analysed. 223 Subjects were enrolled at 101 centres based on indication and therapy requirements according to the German Physician's Circular and Summary of Product Characteristics (age ≥18 y., ID based on chronic IBD, therapeutic necessity for iron substitution). All patients were ferinject®-naïve.
**Results:** Of 223 subjects (127 CD; 97 UC) treated, 193 patients who received at least one dose of FCM were included in the safety analysis, and 150 in the efficacy evaluation (Wk 12–14 or study termination). Mean total iron dose was 1,139 mg (range: 100 mg-4,800 mg). 76.7% of doses were between 500 mg and 2,000 mg. No adverse drug reactions, SAEs or deaths were observed. Mean Hb increased from 10.0 to 12.3 g/dL. Normal Hb or improvement ≥2 g/dL was achieved by 63.3% of patients. Ferritin increased from 52$\mu$g/L to 103$\mu$g/L, TSAT from 15% to 25%, and mean serum iron from 6.1 to 12.4$\mu$mol/L. The differences in Hb, ferritin, TSAT and serum iron are statistically significant ($p = 0.0001$). Median single dose was 500 mg FCM, median infusion frequency was 2, median duration was 15 min, median dilution was 250 mL. Clinical scores showed that QoL improved due to massive reduction of symptoms of anaemia.
**Conclusion:** Ferinject®-therapy has proven to be effective and safe in a large cohort of patients with IBD-associated anaemia in routine daily practice, and provides a sufficient refill of iron stores. These results are similar to those obtained from controlled clinical trials. Rapid, high-dose application offers increased convenience for physicians and reduces patients' time lost from work.
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S. Weber-Mangal: Susanne Weber-Mangal is an employee of Vifor Pharma
K. Nip: Kerry Nip is an employee of Vifor Pharma
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All other authors have declared no conflicts of interest.

## P0883 BIOLOGICAL THERAPY FOR IBD IN THE ELDERLY: SENSE, SCIENCE OR SENSIBILITY?

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**Introduction:** The role of biological therapies in the decisive induction and maintenance of remission of moderate-severe inflammatory bowel disease (IBD) is established through pivotal trials. There is a lack of data on their use in older patients.
**Aims & Methods:** Our aim was to review the use of biological therapy in older IBD patients at our institution, including patient demographics and adverse events. We conducted a retrospective study of patients aged 60 and above with IBD treated with a biological agent atour institution. Data was collected using electronic case records and included demographics, disease characteristics (Montreal classification), treatment and adverse events.
**Results:** Of 47 patients who were treated with a biologic, 24 were male. The median age at diagnosis of IBD was 60 (range 26–84) and the median age at most recent follow up was 70 (range 60–86). Twenty six patients had Crohn's disease (CD), 19 had Ulcerative Colitis (UC) and 2 IBD Unclassified (IBDU). Disease classification was as follows: CD-L1(7), L2 (9) and L3 (10). 20 patients had B2 disease. For UC-E1 (2), E2 (9) and E3 (8). At most recent review 42 patients were still receiving a biological agent, 16 were on Adalimumab, 25 on Infliximab and 1on Vedolizumab. Of the 5 patients no longer on a biologic all had received Infliximab. The mean duration betweendiagnosis of IBD and commencement of biological agent was 98 months (range 0–480) at a median age of 66 (range 53–84). At most recent follow up 18 patients were on a concomitant immunomodulator; 16 were on Azathioprine and 2 on Methotrexate. Of 16 patients on Adalimumab, 14 had prior Infliximab and were switched due to adverse drug reactions (Leucopenia (1), Infusion reaction (3), Other (4)), patient convenience (4) or inadequate response (2). One patient had Vedolizumab following reactivation of pulmonary TB on Infliximab. Another patient treated with Infliximab died from Cryptococcalmeningitis. Sixteen patients had prior IBD related surgery; 5 had surgery after starting a biologic. On most recent follow up 16 patients had active symptoms and 20 patients had evidence of endoscopic remission or improvement with another 9 still demonstrating moderate or severe disease.
**Conclusion:** Data on Anti-TNF therapy in older patients with IBD are conflicting and may reflect disparate practice evenwith comparable disease severity. There is an urgent need for real world data and consensus guidelines enablingclinicians to make personalised decisions (as evidence based as possible) in the holistic, considered and optimalmanagement of older patients with IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0884 COMPARISON OF THE EFFECTIVENESS AND COMPLICATIONS OF INFLIXIMAB AND ADALIMUMAB IN COMBO THERAPY WITH IMMUNOMODULATORS FOR CROHN'S DISEASE

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**Introduction:** TNF$\alpha$ antagonists are currently the most effective therapy for induction and maintenance of remission in Crohn's disease (CD). However, their beneficial effect is not uniform and both the relapses and adverse events may lead to early termination of therapy. There are still doubts what treatment strategy is the most effective.
**Aim:** Comparison of the effectiveness and complication rate of one-year therapy with infliximab (IFX) and adalimumab (ADA) combined with immunomodulators.
**Materials and Methods**: The prospective one-center study included 55 patients (24 females) enrolled in 2014–2015 into Polish National Programme of biologic therapy for CD who failed to respond to conventional therapy (44.8%), showed drug-related side effects (24.1%) or presented perianal fistulas (31%). Nearly all patients received corticosteroids before considering biologics and all patients were treated with immunomodulators (azathioprine or 6-mercaptopurine). Forty-one patients (75%) received IFX and 14 (35%) received ADA. The effect of treatment was assessed with clinical, laboratory, and endoscopic response.
**Results:** There were no differences between IFX and ADA in subjective response to treatment: improvement was reported respectively in 70.8% and 50% of patients, no change in 12.5% and 33.3% of patients and exacerbation was experienced by 16.7% and 16.7% of patients ($p = 0.3$). The Crohn's Disease Activity Index significantly decreased in both groups after one-year therapy (from 342 to 165 in IFX, $p = 0.02$ and from 427 to 73 in ADA group, $p = 0.04$. CRP levels decreased in IFX treated patients (from 22.5 to 9.7 mg/dl; $p = 0.02$); but not in ADA group (from 17.1 to 11.5 mg/dl; $p = 0.3$). Hemoglobin concentration increased after termination of therapy only in IFX group (from 12.6 to 13.7 g/dl, $p = 0.001$) as well. Improvement in endoscopic lesions were detected in similar percentage of patients (56% in IFX and 83% in ADA group, $p = 0.2$). Mucosal healing was achieved in comparable number of patients (25% in IFX and 33% in ADA group, $p = 0.7$). Similar number of patients terminated therapy before scheduled time (22% in IFX and 29% in ADA groups, $p = 0.6$). There were no significant differences between IFX and ADA groups in adverse events: viral infection occurred in 8.3% and 7.7%, bacterial infection in 12.5% and 16.7%, fungal infection in 4.2 and 0%, tuberculosis in 4.2% and 0%, anemia in 25% and 23.1%, leucopenia in 8.3% and 15.4%, liver dysfunction in 4.2% and 7.7%, and fever in 16.7% and 30.8% of patients. Four patients in IFX group and one in ADA group required surgery during biologic therapy ($p = 0.4$).
**Conclusion:** These data demonstrate similar effectiveness and safety of combo one-year therapy with IFX and ADA. Efficacy of both regimens was proved by reduced disease activity, decreased inflammatory biomarkers and improved blood count. Deep remission was achieved in 1/4 of infliximab and 1/3 of adalimumab treated patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00
**PAEDIATRIC: LOWER GI – POSTER EXHIBITION**

## P0885 A STRUCTURED PAEDIATRIC TO ADULT TRANSITION SERVICE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE REDUCES DISEASE FLARES, REQUIREMENT FOR STEROIDS AND EMERGENCY ADMISSIONS: THE TRANSIT STUDY

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**Introduction:** Inflammatory bowel disease (IBD) presents in childhood/adolescence in up to 25% of patients. Guidelines recommend structured paediatric to adult transition when moving patients to adult IBD services; however, there is little published objective data on the benefits of such a structured transition programme.
**Aims & Methods:** The primary aim of TRANSIT was to compare the impact of structured transition vs. no transition on measurable, objective indicators of disease control. A retrospective case note review and cross-sectional patient survey of outcomes following the first visit involving the adult IBD services (the index visit) was conducted in 11 UK centres. Eligible patients with a confirmed diagnosis of IBD before age 16 years who were subsequently under the care of adult services for 12–36 months were recruited. 'Transition patients' had attended ≥2 structured transition service visits and 'non-transition patients' had not attended any transition visits. Predefined outcome measures included IBD disease flares (defined as any Crohn's disease [CD] or ulcerative colitis [UC]-related hospitalisations, or increase in CD/UC therapy), steroid treatment and hospital visits/admissions. Data were collected for the 12-month period before

(pre-index) and after (post-index) the index visit. Patients completed 7 questionnaires at the point of recruitment.
**Results:** The study recruited 95 transition patients (median age 19.6 [interquartile range (IQR): 18.7–21.0] years; 47% female; 78% CD; median of 2.0 (IQR: 2.0–3.0) transition visits; median 2.1 [IQR: 1.4–3.2] years since index visit) and 34 non-transition patients (median age 19.3 [IQR: 18.2–21.3] years; 41% female; 74% CD; median 2.3 [IQR: 1.5–4.5] years since index visit). Most patients were in remission in the pre-index period, with 24 transition patients (25%) and 13 non-transition patients (38%) having ≥1 flare; post-index, 27 transition patients (28%) and 16 non-transition patients (47%) had ≥1 flare ($p > 0.05$). The mean number of flares/patient were similar in transition (0.4 [standard deviation (SD): 0.9]) and non-transition patients (0.4 [SD: 0.8]) pre-index, but significantly different post-index (non-transition: 1.0 [SD: 1.4] vs. transition: 0.6 [SD: 0.9]; $p < 0.05$). Mean flares/patient post-index were significantly different in females (transition: 0.4 [SD: 0.8]; non-transition: 1.2 [SD: 1.5]; $p < 0.05$) but not males (transition: 0.5 [SD: 0.9]; non-transition: 0.9 [SD: 1.4]; $p > 0.05$). Post-index, 67/95 transition patients (70.5%) remained steroid-free compared with 14/34 non-transition patients (41.2%; $p < 0.05$). Hospital visits/admissions pre-index were similar in transition and non-transition patients. However, significantly more non-transition patients had A&E visits leading to admission compared with transition patients post-index (see table). There were significantly fewer non-transition patients with post-index outpatient visits compared to transition patients. Patient-reported measures were similar in transition and non-transition patients.
**Conclusion:** These data suggest that adolescent patients undergoing structured transition to adult IBD services have a reduction in IBD flares, are more likely to remain in steroid-free remission and are less likely to have an emergency admission during the first 12-months post-index compared with patients not receiving structured transition care. This dataset is supportive of the current guidelines recommending transition as an integral part of adolescent IBD care.
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## P0886 ACCELERATED STEP-UP APPROACH AND LONG-TERM DISEASE OUTCOMES IN PAEDIATRIC PATIENTS WITH CROHN'S DISEASE

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**Introduction:** The use of accelerated step-up or anti-TNF before first remission and after or in combination with immunomodulators (IM) remains controversial in paediatric Crohn's disease (CD).
**Aims & Methods:** Five-year follow-up data from BELCRO (Belgian observational prospective cohort of paediatric CD) were analysed. Disease severity was scored as inactive, mild or moderate-to-severe on a 3-point scale based on PCDAI and/or PGA scores at diagnosis and monitored yearly. Univariate analyses were performed between patients treated with anti-TNF before or after first remission and correlations were assessed between treatment variables and the outcomes average disease severity and sustained remission, defined as inactive disease for ≥ 2 yrs follow-up.
**Results:** Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5 – 15.2) yrs, 50% male), 47% had accelerated step-up and 5% never reached remission. Accelerated step-up was associated with older age (13.3 (12.1 – 15.9) vs. 12.5 (10.2 – 14.1) yrs; $p = .02$), higher average disease severity (1.8 (1.6 – 1.9) vs. 1.6 (1.3 – 1.8); $p < .01$) but similar disease location and severity at diagnosis compared to anti-TNF after first remission. Delay to steroids and IM and duration of steroids was similar in both groups, but delay to anti-TNF or combination therapy and duration of IM was shorter with anti-TNF before first remission, resulting in longer duration of anti-TNF but similar duration of combination therapy. Time to first remission was longer in the accelerated step-up group but delay to and duration of sustained remission was similar in both groups.

Univariate analyses of treatment and outcome variables between patients treated with anti-TNF before or after first remission (no correction for multiple testing).

| Treatment or outcome variable, median (IQR) in yrs | Anti-TNF before first remission (n = 31) | Anti-TNF after first remission (n = 32) | P value |
|---|---|---|---|
| Delay to first steroids | 0 (0 – 0.05) | 0 (0 – 0.01) | .60 |
| Duration of steroids | 0.4 (0.3 – 0.6) | 0.4 (0.3 – 1.0) | .96 |
| Delay to first immunomodulator | 0.08 (0.01 – 0.16) | 0.09 (0.01 – 0.46) | .55 |
| Duration of immunomodulator | 2.0 (1.2 – 2.7) | 3.9 (2.0 – 4.8) | **.02** |
| Delay to first biological | 0.6 (0.4 – 0.9) | 2.1 (1.4 – 3.3) | < **.0001** |
| Duration of biological | 4.6 (4.0 – 4.9) | 2.7 (1.6 – 3.6) | < **.0001** |
| Delay to combination | 0.6 (0.2 – 1.0) | 2.4 (1.5 – 3.5) | < **.0001** |
| Duration of combination | 1.0 (0.5 – 2.0) | 1.3 (0.6 – 2.1) | .57 |
| Time to first remission | 1.5 (1.1 – 3.0) | 0.5 (0.3 – 0.8) | < **.0001** |
| Time to sustained remission | 3.1 (2.6 – 4.0) | 2.7 (2.0 – 3.6) | .14 |
| Duration of sustained remission | 2.1 (1.4 – 4.0) | 2.7 (1.3 – 4.6) | .45 |

Rates of surgery and hospitalisations for CD were similar and at 5 yrs, inactive disease (68% vs. 69%, $p = .93$) was similar and IM use (24% vs. 59%; $p < .01$) lower in the group treated with anti-TNF before first remission. Accelerated step-up correlated with average disease severity (AUC = .70; $p < .01$) but not sustained remission (no correction for multiple testing). No other correlations were found between treatment and outcomes.
**Conclusion:** Accelerated step-up was prescribed for more severe disease and in older children not remitting on IM. IM exposure was limited compared to anti-TNF upon relapse despite IM. Only patient age was associated with initial response to IM. Sustained remission was similar for all children needing anti-TNF.
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**Abstract No: P0885**

**Table:** Hospital visits and admissions before (pre-index) and after (post-index) the initial visit involving adult IBD services

| | 12-months pre-index | | 12-months post-index | |
|---|---|---|---|---|
| | Transition(n = 95) | Non-transition(n = 34) | Transition (n = 95) | Non-transition(n = 34) |
| A&E visits (all)*A&E → admission* | 8% (n = 8)*5% (n = 5)* | 9% (n = 3)*9% (n = 3)* | 8% (n = 8)*5% (n = 5)* | 18% (n = 6)*18% (n = 6)** |
| Inpatient admissions (all)*Flare-related* | 13% (n = 12) *5% (n = 5)* | 24% (n = 8)*24% (n = 8)* | 13% (n = 12) *8% (n = 8)* | 21% (n = 7)*18% (n = 6)* |
| Day case (all) | 45% (n = 43) | 47% (n = 16) | 27% (n = 26) | 26% (n = 9) |
| Outpatients (all) | 94% (n = 89) | 94% (n = 32) | 94% (n = 89) | 74% (n = 25)* |

Data presented as the % (n) of patients with each hospital visit. *$p < 0.05$ comparing transition and non-transition patients in the 12-months post-index period

## P0887 THE ASSOCIATION BETWEEN PEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE AND BONE MINERAL DENSITY IN ADULTHOOD

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**Introduction:** Inflammatory bowel disease (IBD) is known to pose a risk for low bone mineral density (BMD) in both children and adults.

**Aims & Methods:** We aimed to evaluate the impact of pediatric-onset IBD on BMD in adulthood. Records of patients diagnosed with pediatric IBD were retrospectively reviewed. Patients who had documentation of dual energy X-ray absorptiometry (DXA) scans after the age of peak bone mass accrual (females-18 years, males- 20 years) were included. BMD was expressed as z-score and defined as the lower between lumbar and femoral-neck BMD for each patient.

**Results:** 61 patients with pediatric-onset IBD were included. Median age at diagnosis was 15.3 years (IQR 14–16.5). Median age at first DXA scan in adulthood was 21.9 years (IQR 20.2–27.3). Mean BMD z-score was −1.12 (±1.04). Overall, 44.3% (n = 27) had osteopenia (BMD z-score ≤ -1), and 8.2% (n = 5) had osteoporosis (BMD z-score ≤ -2.5). This deviation from normal distribution of BMD was statistically significant ($p < 0.001$). Bone status showed no correlation with age, disease severity, height z-score and vitamin D status at diagnosis, type of IBD or duration of disease. Significant correlation ($r = 0.306$, $p = 0.05$), was identified between low weight z-score at diagnosis and abnormal bone status in adulthood. Thirty six patients had at least 2 DXA scans during follow-up. During a median interval of 3.6 years there was no significant change in BMD between first and last measurement.

**Conclusion:** Osteopenia and osteoporosis are frequent in adult IBD patients with pediatric-onset disease. BMD does not significantly change over time in these patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0888 REMISSION INDUCTION IN CORTICOSTEROID-NAÏVE CHILDREN AND ADOLESCENTS WITH ACTIVE ULCERATIVE COLITIS BY ADSORPTIVE LEUCOCYTAPHERESIS AS MONOTHERAPY OR IN COMBINATION WITH LOW-DOSE PREDNISOLONE AFTER FAILURE OF FIRST-LINE MEDICATIONS

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**Introduction:** In patients with active ulcerative colitis (UC), myeloid lineage leucocytes are known to show activation behaviour and increased survival time, including the CD14+CD16+ monocyte phenotype, which releases tumour necrosis factor-$\alpha$. Therefore, selective depletion of myeloid leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with an Adacolumn should promote remission, or enhance drug efficacy. Potentially, GMA should be a relevant option in paediatrics and adolescents in whom drug therapy has limitations.

**Aims & Methods:** This study was to evaluate the efficacy of GMA in children and adolescents with active UC in whom conventional first-line medications had failed. Between 2010 and 2015, a total of 30 consecutive patients, age 11–19 years, body weight 33–55.5 kg were given mesalazine (n = 23) or sulphasalazine (n = 7) as a first-line medication. Twenty patients relapsed or did not respond and received GMA with the Adacolumn, 2 sessions in the first week, then weekly, up to 11 sessions. Patients who achieved a decrease of ≥5 in the clinical activity index (CAI) continued with GMA while non-responders received GMA in combination with prednisolone (PSL). At entry and week 12, patients were clinically and endoscopically evaluated, allowing each patient to serve as her or his own control.

**Results:** At entry, all 30 patients were corticosteroid naïve and none had deep UC lesions together with extensive loss of the mucosal tissue at the affected sites. Ten patients achieved stable remission with the first-line medications and did not receive GMA. Six patients did not respond well to the first 5 GMA sessions and received PSL (0.5 to 1.0 mg/kg bodyweight) together with GMA, while 12 patients responded well to GMA with stable remission and 2 withdrew from GMA to receive high dose PSL (up to 2 mg/kg bodyweight). At entry, the average CAI was 14.2 ± 0.4 (n = 28), range 11–17, and the average endoscopic index was 9.2 ± 0.4, range 7–11. The corresponding values at week 12 were 2.1 ± 0.2, range 1–4 ($P < 0.001$) and 2.4 ± 0.2, range 1–4 ($P < 0.001$). PSL was tapered to 0 mg within 3 months. Therefore, at week 12, all 30 patients were in clinical remission, majority with mucosal healing (complete remission).

**Conclusion:** In the past, GMA in patients with deep ulcers and extensive loss of the mucosal tissue (a major GMA non-responder feature) has not been associated with significant efficacy. In this study, GMA in young corticosteroid naïve patients with active UC refractory to the first-line medications was associated with clinical remission and mucosal healing, while in non-responders to GMA monotherapy, addition of a low dose PSL enhanced the efficacy of GMA and tapering of the PSL dose was not associated with UC relapse. Therefore, the majority of young steroid-naïve UC patients who fail to respond to first-line medications should respond well to GMA and be spared from pharmacologicals. Additionally, GMA has a good safety profile, which is a favourable feature in clinical practice setting.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0889 PREDICTING DISEASE COURSE OF PEDIATRIC CROHN'S DISEASE: ROLE OF CLINICAL, ENDOSCOPIC AND IMAGING FINDINGS AT THE DIAGNOSIS

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**Introduction:** Identifying the factors related to a more severe disease course in pediatric Crohn's disease (CD) may lead to an optimal and individualized use of therapeutic options and possibly to a change in the natural history of the disease.

**Aims & Methods:** Aims of this study were to evaluate the predictive value of clinical, laboratory, endoscopic and imaging factors at the diagnosis for the risk of surgery and complicated disease course in children with CD. In this single-centre, prospective, longitudinal study, children newly-diagnosed with CD were enrolled and followed for 3 years. At baseline all patients underwent a clinical evaluation (Pediatric Crohn Disease Activity Index, PCDAI), laboratory exams (including C-Reactive Protein [CRP] and Erythrocyte Sedimentation Rate [ESR]), Magnetic Resonance Imaging (MRI) and ileocolonoscopy. Disease location and behavior were defined by Paris classification[1]. Simple endoscopic score for Crohn's disease (SES-CD)[2] was used to evaluate the severity of endoscopic lesions. Rate of surgery at maximum follow up was the primary outcome evaluated.

**Results:** Fifty patients (64% males, median age 12.7 ± 2.9 years) were enrolled. Mean SES-CD at the diagnosis was 15.3 ± 10.6. A SES-CD graded as severe (> 15) was present in 20/50 (40%) patients. MRI showed ulcers in 7/50 (14%) patients, stenosis in 20/50 (40%), pre-stenotic bowel dilation in 14/50 (28%), abscesses in 3/50 (6%) and fistulas in 7/50 (14%). The presence of stenosis at ileocolonoscopy ($p = 0.009$) and fistulae at MRI ($p = 0.05$) correlated with the need of resection surgery at follow-up. At a multivariate analysis, penetrating disease [r 0.65(0.40 to 0.81);$p < 0.0001$], perianal involvement [0.41 (0.15 to 0.62);$p = 0.002$], stenosis at ileocolonoscopy [r 0.30 (0.03 to 0.53);$p = 0.02$] and fistulas at MRI [r 0.41 (0.15 to 0.62);$p = 0.002$] at the diagnosis increased the surgical risk at follow-up, while inflammatory behavior (B1 according to Paris classification) (r −0.4 (−0.6 to −0.1); $p = 0.006$) and ESR > 25 mm/h (r −0.3 (−0.5 to −0.03); $p = 0.03$) were negatively associated.

**Conclusion:** Penetrating behavior at the diagnosis and perianal disease along with the presence of stenosis at ileocolonoscopy and fistulas at MRI are independent predictive factors of the surgical risk in children with CD. An inflammatory behavior and high ESR seem to correlate with a milder disease course

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0890 THE CLINICAL BURDEN OF TRANSITION IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** Transition in inflammatory bowel disease (IBD) is a planned movement of adolescents from paediatric to adult services. Most work focuses on engagement of the patients, encouragement of effective communication and awareness of the surrounding psychosocial factors and patient experience of transition. The data on clinical outcomes is sparse, although clearly important in a high-risk population who already have one poor prognostic risk factor: age.
**Aims & Methods:** We aimed to assess the clinical changes taking place during the 12months after transition. Adolescent patients diagnosed in pediatrics and transitioned to New Cross Hospital adult IBD service, UK between 2009–2015 were identified and notes retrospectively reviewed for a 12 month follow up period.
**Results:** 28 patients were included for analysis, with a median age of 16.8 at time of first adult clinic. The average transition interval was 143 days. 12 had ulcerative colitis (UC), of whom 8 had pancolonic disease. 8 of 16 patients with Crohn's Disease (CD) had perianal disease and 2 had surgery pre-transition. Eight of the 28 suffered extraintestinal manifestations of IBD. Twenty-five of 28 had been treated with steroids and 21 with a second-line immunomodulator. 11 CD patients had been exposed to one or more biologic. At the time of transition 11 were reported and handed over with active disease. 4 patients were assessed in a joint clinic. This group then had a total of 165 outpatient appointments between them in 12 months, 14 patients having between 1–4 each and 14 having between 5–10 each. The number of did not attend (DNA) appointments were 64 (39%). Within 12 months of adult transition 14 had MRI scans, 17 had endoscopy procedures. 14 CD and 8 UC patients required pharmacological escalation of IBD therapy (Table 1). 6 required surgery and 5 had medical hospital admissions. After 12 months of adult transition 22 patients were deemed to be in clinical remission.

12 Month Post Transition Outcomes

| | UC | CD | Overall | p-value |
|---|---|---|---|---|
| **n** | 12 (43%) | 16 (57%) | 28 | |
| **Clinics within 12 months** | 4 | 5.2 | 4.7 | 0.14 |
| **Steroids** | 4 (33%) | 7 (44%) | 11 (39%) | 0.57 |
| **Surgery** | 0 | 6 (38%) | 6 (21%) | 0.02 |
| **Admissions** | 1 (8%) | 3 (19%) | 4 (14%) | 0.61 |
| **Medical Escalation of IBD therapy** | 8 (67%) | 14 (88%) | 22 (79%) | 0.13 |
| **Immunomodulator dose escalation** | 3/9 (33%) | 4/15 (27%) | 7/24 (29%) | 0.10 |
| **Immunomodulator introduction** | 2 (17%) | 2 (13%) | 4 (14%) | 1.00 |
| **Biologic dose escalation** | 0 | 3/9 (33%) | 3/9 (33%) | 0.51 |
| **Biologic introduction** | 1 (8%) | 3 (19%) | 4 (14%) | 0.61 |
| **Active IBD (at last paediatric clinic)** | 3 (25%) | 8 (50%) | 11 (39%) | 0.25 |
| **Active IBD (12 months after first adult clinic)** | 1 (8%) | 5 (31%) | 6 (21%) | 0.19 |
| **Clinic DNA within 12 months** | 5 (42%) | 6 (38%) | 11 (39%) | 1.00 |

**Conclusion:** Adolescents have a high burden of disease and despite being handed over in an apparent state of remission, rates of requirement for pharmacological escalation and surgical intervention remain high. Engagement remains an issue. A more formalised process of clinical transition is required between pediatric and adult units to maximise clinical disease management and stability while moving them to an environment where engagement, developmental maturity, abstract reasoning, helicopter parenting etc are all complex factors in this small but heavily burdened group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0891 PEDIATRIC CROHN'S DISEASE AND ITS DISABILITY OVER TIME: A STUDY PERFORMED WITH A NEW PEDIATRIC LÉMANN INDEX. PRELIMINARY DATA FROM A TERTIARY PEDIATRIC IBD CENTER

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**Introduction:** Crohn's disease (CD) is a chronic and progressive condition that, due to disease complication, leads to surgical resection in the majority of cases. Recently, a panel of expert developed the Lémann Index (LI), a new tool aimed to assess the progressive bowel damage due to disease course. The aim of LI is to assess structural bowel damage due to CD based on stricturing lesions, penetrating lesions and surgical resection. However, in the pediatric population we should also take into account also peculiar characteristics, such as intestinal length and the pattern of growth of the patient.
**Aims & Methods:** The aim of our study was to measure the LI in a pediatric cohort at diagnosis as well as the trend of LI during time. We chose segments of 10 cm for small bowel, instead of 20 cm as proposed in adults. Moreover, we decided to adjust the final score considering growth failure, using different values based on weight and height at diagnosis and at the last evaluation. We called this new score pediatric LI (P-LI).
We retrospectively selected 47 consecutive pediatric patients who were firstly diagnosed at our hospital by abdominal Magnetic Resonance Imaging, colonoscopy and upper GI endoscopy, and in case of perianal disease, a pelvic magnetic resonance immaging. Patients were aged between 6 to 17 years. We evaluated the P-LI at diagnosis and calculated the difference between P-LI at diagnosis and at the last pediatric outpatient visit or at transition to adult outpatient.
**Results:** We included a total of 47 CD pediatric patients (23 male, median age 18 years, range 11–27, median age at diagnosis 12 years, range 7–17) who were followed-up for a median of 41 months (range 4–120). Among them, 30 (63.8%%) patients had a stable P-LI during the follow up, whereas 17 (36.2%) had an increase in P-LI during time. Considering the overall population there was no statistical significant difference between median P-LI at beginning and at the end of follow-up (4.6, range 0.6–15 vs 3, range 0.3–31.7. $P = 0.064$). Subdividing patients who underwent surgical resection ($n = 12$, 25.5%) and those who did not ($n = 35$, 74.5%) we found a significant difference between median P-LI at the beginning and at the end of follow up in both groups (4.4, range 1–12.8 vs 15.3, range 8.3–31.7, $P = 0.0002$; 4.6, range 0.6–15 vs 1.6, range 0–18.5, $P = 0.001$) with a disease regression in the no surgery group. Moreover, analyzing data from patients who utilized anti-TNF therapies ($n = 22$, 46.8%), we found no significant difference between LI at the beginning and at the end of follow-up (5, range 1–15 vs 4.2, range 0.6–12.8, $P = 0.3$).
**Conclusion:** Our data suggest that the P-LI we devisd is a useful tool to evaluate CD in the pediatric population and to assess disease progression. In children avoid a surgical resection is extremely important because medical therapy is able to reverse the disease progression
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0892 OUTCOMES AND DETERMINING FACTORS OF A TRANSITION CLINIC PROGRAM FOR INFLAMMATORY BOWEL DISEASES (IBD) BETWEEN 2 ITALIAN TERTIARY CARE CENTERS

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**Introduction:** Transition clinic programs for inflammatory bowel disease (IBD) is an emerging challenge nowadays, however few models have been proposed for a better management of transition-IBD and few information exists on determining factors for successful experiences.
**Aims & Methods:** Aim of our study was to evaluate efficacy of the adopted transition model. Secondary end points were to evaluate predictive factors of success/failure and to evaluate retrospectively the transition program. Proposed model is based on three meetings every four-six weeks: the first in pediatric centre (Bambino Gesù Children's Hospital); the second in the adult centre (Agostino Gemelli General Hospital), with pediatric gastroenterologists; the last in the adult centre with only adult gastroenterologists. During the first visit, the pediatric gastroenterologist proposes the transition; the second time pediatric gastroenterologist presents patient to adult gastroenterologist; in the third meeting, adult gastroenterologist proposes the own follow up program. Questionnaires (General, GQ, transition clinic, TCQ, IBD yourself, self efficacy, VAS based) were used. About nine months after the transition, we made a telephone follow-up and contacted patients who have visited at least once the transition clinic at the Agostino Gemelli General Hospital. Inclusion criteria were: patients with ulcerative colitis (UC) or Crohn's disease (CD) with low disease activity or remission. Transition was considered successful if three steps were reached form patients.
**Results:** Twenty patients were enrolled; age 18–25 years (mean age 20.2, M/F 12/8; UC/CD 10/10); eleven/20 (55%, 8 M/3 F) immediately accepted the second check at adult gastroenterology centre; 5 patients refused transition and 4 patients delayed the transition. Three patients (F)/11 refused follow up in the proposed centre. In eight patients (40%, 8 M) this model was successful. Based on questionnaires, patients elegible referred to be independent and ready to be transferred. They reached high scores in the self-efficacy scale. They appeared to have a good level of knowledge on IBD but low scores about treatments. Young patients who interrupted the transition program felt more independent at VAS-based questionnaire, they totalized higher scores in the self-efficacy scale and referred lower levels of confidence in adult gastroenterologist. Patients who completed the transition program totalized higher scores in the resilience scale, had better scores of wellbeing perception and had lower anxiety scores. Patients who failed the transition program were mostly women. The perceived utility of the transition program was scored 7.3 on a VAS scale. 90% of contacted patients was glad to have had this experience and would repeat it or suggest it.
**Conclusion:** Proposed transition program seems to be feasible. Patients resistant or failing were more likely female, with high self-efficacy scores, lower confidence in adult gastroenterologist and worse wellbeing perception. Psychological

scores together with a systematic approach could help in selecting patient more difficult to candidate to the transition program.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0893 FREQUENCY, CHRONOLOGICAL ORDER OF APPEARANCE AND ANTI-TNF TREATMENT OF EXTRAINTESTINAL MANIFESTATIONS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** There is a paucity of data on the prevalence, type, chronological order of appearance, and treatment of extraintestinal manifestations (EIM) in pediatric patients with inflammatory bowel disease (IBD).
**Aims & Methods:** Since 2008, the Pediatric Swiss IBD Cohort Study has collected data on the pediatric IBD population from university centers (5), community hospitals (4), and private practices (2) across Switzerland. Data on 329 patients (173 with CD, 156 with UC/IC) were analyzed.
**Results:** A total of 55 patients (16.7%) suffered from at least one EIM (39 CD, 12 UC and 4 IC patients). Median IBD duration was 5.2 years (range 0.9–15.1). Of the 55 patients, 39 (70.9%), 12 (21.8%), three (5.5%) and one patient (1.8%) experienced one, two, three and four EIM, respectively. Prevalence of EIM was significantly lower than that observed in the adult IBD population (16.7% vs. 29.3%, $p < 0.001$). (1) EIM were more frequently observed in CD patients (39/173, 22.5%) when compared to UC/IC patients (16/156, 10.3%, $p = 0.003$). The most prevalent EIM were peripheral arthritis (47.3%) and aphthous stomatitis (43.6%) followed by uveitis (10.9%), erythema nodosum (EN, 9.1%) and axial spondylarthropathy (AS, 9.1%). While 28.9% of all EIM appeared before the diagnosis of IBD, the majority of EIM occurred once IBD diagnosis was established (53.9%). The remaining proportion of EIM appeared at the time of IBD diagnosis. Peripheral arthritis, uveitis, pyoderma gangrenosum (PG) and psoriasis were significantly more likely to occur after IBD diagnosis than before. The median time between IBD diagnosis and occurrence of EIM was 1 month (range −37.5 – 149.0). Thirty-one of the 55 patients with EIM (56.4%) were treated with one or more anti-TNF agents (a total of 41 anti-TNF treatments). IBD patients with EIM were more likely to be treated with anti-TNF compared to those without EIM (56.4% vs. 38.6%, $p = 0.013$). However, in only 3 cases, anti-TNF was started for management of EIM. Under anti-TNF treatment, 23 EIM appeared in 19 patients (61.3%) with most of them showing improvement or stable disease course with continuation of anti-TNF. Peripheral arthritis and uveitis showed good clinical response rates to anti-TNF (61.5% and 66.7%, respectively), while those of the other EIM were ≤50%.
**Conclusion:** In a cohort of pediatric IBD patients, EIM were frequently encountered; however, prevalence seems to be lower than that observed in the adult population. The majority of EIM occurred after diagnosis of IBD. EIM were more likely to be observed in CD patients when compared to UC patients. The most frequent EIM were peripheral arthritis and aphthous stomatitis. Anti-TNF were more likely to be started in patients with EIM when compared to those without EIM. Response rates to anti-TNF strongly depended on underlying EIM and were best for peripheral arthritis and uveitis. Development of EIM under anti-TNF treatment was frequent, although disease course was usually benign.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0894 ACCURACY OF IMAGING SCORING INDEXES IN PAEDIATRIC CROHN'S DISEASE PATIENTS

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**Introduction:** Crohn's disease (CD) is a chronic inflammatory disorder that affects the gastrointestinal tract, predominantly involving the small intestine and colon. Up to 66% of patients with Crohn's disease have small-bowel involvement at diagnosis. In approximately 90% of patients with small-bowel Crohn's disease, the disease involves the terminal ileum. Ileocolonoscopy is gold standard in diagnosis of ileocolonic disease but skip lesions and proximal involvement can be evaluated only be meaning of capsule endoscopy (VCE) and or MR enterography (MRE).
**Aims & Methods:** Our aim was to correlate findings obtained from MRE and VCE with Paediatric Crohn's disease Activity Index (PDCAI) at the time of disease presentation. At single-centre, tertiary care hospital centre we prospectively enrolled consecutive paediatric patients with newly diagnosed Crohn's diseases admitted to the Department of Pediatrics in Clinical Hospital Centre Rijeka from December 2010 to December 2015. All the patients had undergone upper and lower endoscopy in deep sedation. PCDAI was made at the time of admission. All patients after endoscopy investigation with suspected small bowel involvement underwent MRE and VCE. MRE and VCE findings were evaluated by using Crohn disease MRI index (CDMI) score and the Capsule Endoscopy Crohn's Disease Activity Index (CECDAI or Niv score) respectively. VCE was performed using PillCam SB 3 with Rapid software. MR enterography protocol was performed on 1.5 T MRI system with combined built in spine array coli and two wrapped around flexible surfce coils. We performed next sequences: HASTE (ST = 100 mm), true FISP: +FS/-FS, HASTE: +FS/-FS; ST = 6 mm, true FISP (axial), DWI, after contrast administration (Gadolinium), VIBE and true FISP, T1. Statistical analysis were performed using Spearman's coefficient of rank correlation.
**Results:** A total of 38 patients, 13 girls (34.2%), median age 14 (95%CI 13–15) were evaluated. During the VCE examination, cecum was reached in all patients. According to PCDAI, 11 patients (28.9%) had inactive disease, 17 (44.7%) had mild disease, while 5 (13.1%) had moderate and 5 (13.1%) severe disease. We found statistically significant correlation between PCDAI-CECDAI ($R = 0.595$; 95%CI 0.31–0.77; $P = 0.0003$) and PCDAI-CDMI ($R = 0.501$; 95%CI 0.18–0.72). In addition CECDAI and CDMI have significant correlation ($R = 0.480$; 95%CI 0.18–0.69; $P = 0.0026$).
**Conclusion:** PCDAI is clinically well-established parameter in evaluating disease severity, but with no adequate reliability in detecting mucosal inflammation. Mucosal inflammation can be be assessed with VCE and MRI, which both have statistically significant correlation with clinical activity index.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## TUESDAY, OCTOBER 18, 2016 09:00–17:00
## OTHER LOWER GI DISORDERS II – POSTER EXHIBITION

## P0895 IMPACT OF NF-KB SUBUNIT DELETION ON THE SMALL INTESTINAL EPITHELIAL TRANSCRIPTOME FOLLOWING LIPOPOLYSACCHARIDE TREATMENT OF C57BL/6 MICE

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**Introduction:** Administration of systemic lipopolysaccharide (LPS) induces rapid epithelial cell apoptosis at the small intestinal villus tip in wild-type mice. This response is increased in animals lacking the NF-κB1 subunit and decreased in mice lacking the NF-κB2 subunit[1]. Here we examine the transcriptomic events that underlie LPS induced small intestinal epithelial cell death, and the differences between these genotypes.
**Aims & Methods:** Groups of C57BL/6 (WT), *Nfkb1*$^{-/-}$ and *Nfkb2*$^{-/-}$mice were treated with 125 μg/kg LPS by intraperitoneal injection for 1.5 h, and euthanased by cervical dislocation. Total RNA was isolated from small intestinal mucosal scrapes. RNA sequencing was performed using the Illumina MiSeq platform. Principal component analysis was used to compare the effects of LPS on small intestinal transcriptomics. Differentially regulated genes were identified using DESeq2. $Log_2$ fold changes of +/- > 0.6, and adjusted $p < 0.01$ were considered significant. Pathway analysis was performed using the iPathwayguide platform.
**Results:** Principal components (PC) 1 to 4 showed clear distinction between genotypes. There was also a clear shift as a result of LPS treatment associated with PCs 2 and 3 for WT and *Nfkb1*$^{-/-}$ mice. An LPS associated shift for *Nfkb2*$^{-/-}$ mice was less apparent. Differential gene expression and pathway analysis provided a consistent narrative to PCA analyses. LPS administration resulted in 1253 differentially regulated genes in WT mice. Pathway analysis identified 63 pathways that were perturbed; most significant of which were cytokine-cytokine receptor interaction, MAPK signalling pathway, PI3K-Akt and NF-κB signalling. In *Nfkb1*$^{-/-}$mice, LPS administration caused differential expression of 185 genes and 33 pathways, 13 of which were also perturbed in LPS-treated WT mice. Intriguingly, despite similar pathological phenotypes, the pathways that were most significantly perturbed in WT mice by administration of LPS were not identified in similarly treated *Nfkb1*$^{-/-}$ mice. Administration of LPS to *Nfkb2*$^{-/-}$ mice had minimal impact on the small intestinal transcriptome; only 3 genes (Tnfaip3, Nfkbia and Phlda1) were differentially expressed between untreated

and LPS treated *Nfkb2*$^{-/-}$ mice. As *Nfkb1*$^{-/-}$mice are known to exhibit a spontaneous inflammatory phenotype, we compared the small intestinal transcriptome of untreated WT mice to that of untreated *Nfkb1*$^{-/-}$mice. *Nfkb1*$^{-/-}$ mice had 2361 differentially expressed genes and 70 perturbed pathways compared to WT mice. Of these, 29 pathways were also perturbed in WT mice administered LPS.
**Conclusion:** These data support the findings of morphological studies of LPS induced small intestinal apoptosis, they confirm a transcriptomic basis for resistance to LPS induced small intestinal pathology in *Nfkb2*$^{-/-}$ mice. Transcriptomic responses of *Nfkb1*$^{-/-}$ mice to LPS at first appear blunted compared to WT mice, however, a number of the pathways affected by LPS administration in WT mice are disrupted in untreated *Nfkb1*$^{-/-}$ mice. This reflects the spontaneous inflammatory state of *Nfkb1*$^{-/-}$ mice, which may influence the severity of LPS induced small intestinal pathology in these animals.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0896 FUNCTIONAL AND MOLECULAR ANALYSIS OF THE EFFECT OF OXIDATIVE STRESS AND AGEING ON SMALL INTESTINE AND COLON

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**Introduction:** Reactive oxygen species have been implicated in the pathogenesis of many gastrointestinal (GI) diseases including inflammatory bowel disease (IBD), colitis and associated cancers and possibly linked to gut dysfunction in ageing. How different region of gut react to, and handle elevated levels of free radicals in young and aged is unclear.
**Aims & Methods:** The aim of this study was to examine the effect of oxidants on sensory nerve activity in the small and large intestine of young (3- months) and aged (22- months) mice. We hypothesised that there would be regional differences between small and large intestine in susceptible to oxidative stress. Experiments were conducted in-vitro from jejunum and colon of male C57BL/6 J mice. Epithelial cells were isolated from each segment; RNA was extracted and used to determine differential gene expression in jejunum and colon of young and aged mice by quantitative PCR, $n = 3$. We focused on some members of transient receptor potential (Trp) channels because of evidence for their role in sensing oxidative stress (Trpa1, Trpm2, Trpc5, Trpc6). Dihydroethidium (DHE) dye was used (oxidative marker) on fresh tissue sections from jejunum and colon to evaluate the levels of superoxide anion in aged and young group, $n = 6$. Sensory nerve recordings were performed on isolated jejunum and colon from young and aged mice, data are presented as mean±SEM spikes$^{-1}$ with $n = 6$. Statistical analysis was performed using Student's t-test and ANOVA (two way) as appropriate. $P < 0.05$ was considered as significant.
**Results:** Quantitative PCR analysis indicated deferential gene expressions of oxidative sensors Trpa1 and Trpm2 (4-fold and 2-fold change respectively) in aged colonic epithelial cells compared to young. Higher levels of superoxide anion were found in sections treated with DHE in colon of aged group compared to young (unpaired t-test, $p < 0.007$). Ramp distension of segments of intestine evoked a biphasic increase in afferent discharge, which represents the activation of low threshold (LT), wide dynamic range (WDR) and high threshold (HT) mechanosensitive afferent fibres. Baseline nerve firing remained unchanged in jejunum and colon between young and aged group. Nerve firing in response to distension was attenuated with age only in colon, especially in WDR and HT components between 30 and 60 mmHg, $P < 0.05$. To examine the regional difference in response to oxidative stress, the mitochondrial inhibitor Antimycin A (20 μM) was applied intraluminally to jejunum and colon of young and aged mice. Afferent hyperactivity in response to Antimycin A was observed only in colon of young and aged group. Nerve firing in response to distension was significantly increased by Antimycin A (20 μM), mainly the WDR & HT component ($P < 0.001$). Similarly, baseline nerve activity was enhanced, $P < 0.02$. Trpa1 antagonist HC030031 (30 μM) failed to block the Antimycin A- induced hyperactivity of colonic afferents in young and aged mice.
**Conclusion:** This study suggests that colon is more vulnerable to ageing and responds to oxidants less efficiently than the small intestine. The ability of small intestine to handle oxidants seems to be preserved during ageing. The regional difference between jejunum and colon could be due to chronic accumulation of ROS in the tissue.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0897 THE SUPPRESSIVE EFFECT OF REBAMIPIDE, SUCRALFATE AND RIFAXIMIN ON INFLAMMATION AND APOPTOSIS IN RADIATION INDUCED INTESTINAL INJURY OF MOUSE

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**Introduction:** Radiotherapy for malignant abdominopelvic disease results in radiation-induced enterocolitis. However, there is no well-established preventive strategy. The aim is to evaluate the suppressive effect of rebamipide, sucralfate and rifaximin on ionizing radiation (IR)-induced acute inflammation and apoptosis in the intestine of mouse.
**Aims & Methods:** Thirty ICR mice were divided into (1) a vehicle-treated control group before sham IR, (2) a vehicle-treated group before IR, and (3–5) rebamipide, sucralfate or rifaximin-treated groups before IR. The intestine was resected at 4 hours after 4 Gy IR to the abdominopelvis. Pro-/anti-inflammatory and pro-/anti-apoptotic factors were investigated.
**Results:** NAMPT was down-regulated after IR, which was attenuated by rebamipide, sucralfate and rifaximin ($p < 0.05$). Activation of NF-$\kappa$B and phosphorylation of MAPKs were induced by IR, which were suppressed by rebamipide, sucralfate, and rifaximin ($p < 0.05$). TNF-$\alpha$, IL-1$\beta$, and IL-6 were increased by IR, while attenuated by rebamipide, sucralfate, and rifaximin down to similar level of control group ($p < 0.05$). The iNOS, COX-2 and PGE2 were significantly induced by IR, which were attenuated by rebamipide, sucralfate, and rifaximin ($p < 0.05$). ICAM-1 was corresponded to above mentioned results. [$Ca2^{+}$] oscillation was increased by IR, which was attenuated by rebamipide, sucralfate, and rifaximin. Proapoptotic gene (Bax, c-Myc) and antiapoptotic gene (Bcl-2, Bcl-xL) expressions were potently suppressed and induced, respectively, by rebamipide, sucralfate, and rifaximin. The release of cytochrome C was increased by IR, while it was attenuated by rebamipide, sucralfate, and rifaximin ($p < 0.05$). Caspase 3 and caspase 7 were also elevated by IR compared to control group, however, they showed decline by rebamipide, sucralfate, and rifaximin ($p < 0.05$).
**Conclusion:** This study demonstrated that rebamipide, sucralfate, and rifaximin have the suppressive effects on IR-induced acute inflammation and apoptosis in the intestine of mouse. Rebamipide, sucralfate, and rifaximin may have beneficial effects in preventing acute radiation-induced enterocolitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0898 LOWER GASTROINTESTINAL ENDOSCOPY HAS IMPACT IN THE CLINICAL OUTCOME OF GRAFT-VERSUS-HOST DISEASE

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**Introduction:** Graft-versus-host disease (GVHD) is a common complication after allogeneic hematopoietic cell transplantation (allo-HCT) that mainly affects the skin, the liver and the gastrointestinal tract. When allo-HCT patients develop gastrointestinal manifestations it is critical to establish a diagnosis in order to define the correct therapeutic approach.
**Aims & Methods:** Our aim was to ascertain the role of lower gastrointestinal (LGI) endoscopy and histology in patients with clinical suspicion of gastrointestinal GVHD. We performed a retrospective study from January 2012 to December 2015 that included allo-HCT patients who underwent lower gastrointestinal endoscopy because of de novo digestive complaints suspected to be GVHD. We analyzed demographic, clinical, endoscopic and histologic variables to assess the role of endoscopy and biopsies in the final diagnosis and therapeutic strategy.
**Results:** During the considered period, 275 patients underwent allo-HCT. A LGI endoscopy was performed to 59 of these patients, 55% male, mean age $41 \pm 18$ years. Nearly half (48%) was already diagnosed with GVHD before the onset of gastrointestinal complaints. The digestive manifestations were diarrhea (95%), abdominal pain (35%) and lower GI bleeding (28%); half the patients concomitantly presented with upper GI symptoms. Biopsies were taken in all cases, even in the absence of endoscopic findings (19%). Gastrointestinal GVHD was the histological diagnosis in 66% of the cases, of which 68% (21 patients) were new diagnosis of GVHD. These results led to therapeutic modifications in 59% of the patients, which all had favorable clinical outcomes.
**Conclusion:** In allo-HCT patients with de novo digestive complaints, LGI endoscopy proved to be useful to confirm previously diagnosed GHVD, to exclude other causes of GI symptoms and to identify new cases of GVHD. Lower gastrointestinal endoscopy modified the clinical course of the disease once it motivated therapeutic adjustments in more than half of the patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0899 STROMAL DERIVED FACTOR-1 AS A SEROLOGIC BIOMARKER FOR DIAGNOSIS OF COLON ISCHEMIA WITH CARDIOVASCULAR DISEASE

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**Introduction:** Colon ischemia (CI) is a common form of intestinal ischemia, resulting in severe morbidity occasionally. Until now, specific biological markers to predict early diagnosis of CI have not been identified. We evaluated stromal derived factor-1 (SDF-1) as a new biomarker for CI.

**Aims & Methods:** Serum SDF-1 levels were assessed prospectively in four groups; Group1 healthy controls (n = 13), Group 2, CI with cardiovascular disease (CVD) (n = 23), Group 3 CI without CVD (n = 21) and Group 4 with irritable bowel syndrome (n = 42). The levels of serum SDF-1 were analyzed with ELISA.

**Results:** The serum SDF-1 was elevated in all CI (group 2 and 3) at admission (43.8 pg/mL, range 0.1–454.9), compared with group 1 (0.1 pg/mL, range 0.1–37.65) and group 4 (0.1 pg/mL, range, 0.1- 58.6) ($P = 0.1$) but it was not significantly important. The serum SDF-1 at admission (102.7 pg/mL, range, 0.1–454.9) in group 2 were more elevated than that of group 1 (0.1 pg/mL, range 0.1–37.65), group 4(0.1 pg/mL, range, 0.1- 58.6) and that at admission in group 3 (0.1 pg/mL, range, 0.1- 134.07) ($P = 0.2$). In multivariate regression analysis, CVD showed association with SDF-1 levels ($P < 0.05$).

**Conclusion:** Serum SDF-1 would be a valuable biomarker for diagnosis of colon ischemic with cardiovascular disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0900 ACYL-HOMOSERINE LACTONE QUORUM SENSING MOLECULE ACTIVATES THE BITTER TASTE RECEPTOR, T2R138, IN ENTEROENDOCRINE CELLS

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**Introduction:** Bitter taste receptors (referred as T2Rs) detect bitter taste, a warning signal to protect the organism from harmful food constituents. T2Rs are also expressed in enteroendocrine (EEC) cells and are likely to serve as transducers for the detection of luminal contents. The bitter taste receptor T2R38 acts as sentinel in bacteria recognition to regulate immune defense in the airway, where it is activated by acyl-homoserine lactone (AHL) quorum-sensing molecule, a product of gram-negative bacteria. In the gut, we have shown that T2R38 in humans and its counterpart T2R138 in mouse is upregulated in obesity, which is associated with intestinal dysbiosis and inflammation. In addition, manipulation of gut dysbiosis with antibiotics reversed obesity-induced T2R138 overexpression. Furthermore, there is a high correlation between T2R138 expression and different species of bacteria.

**Aims & Methods:** In this study, we tested the hypothesis that T2R138 in EEC cells senses luminal bacteria or bacterial products by examining whether the bacteria-produced quorum-sensing molecule, AHL, activates downstream signaling effectors associated with T2R138 transduction in mouse STC-1 cells, a model for EEC cells. Specifically, we compared the effect of AHL and the selective T2R138 ligand, phenylthiocarbamide (PTC) on intracellular $Ca^{2+}$ concentration ($[Ca^{2+}]_i$) since we previously showed that PTC induces increase in $[Ca^{2+}]_i$ in different models of EEC cells, including STC 1 cells. STC-1 cells were treated with PTC (0.1–10 mM), or AHL (0.01–0.5 mM) and $[Ca^{2+}]_i$ was measured by calcium fluorometry using fura-2 AM. The T2R138 antagonist, Probenecid and transfection of STC 1 cells with siRNA (10–50 mM) targeting mT2R138 were used to assess whether AHL and PTC activate the same bitter taste receptor pathway.

**Results:** AHL similarly to PTC induced a rapid and transient increase in $[Ca^{2+}]_i$ followed by a slower return to baseline in STC1 cells, effect inhibited by Probenecid. Silencing of T2R138 with siRNA significantly reduced $Ca^{2+}$ signaling in response to 3 mM PTC or 0.1 mM AHL ($p < 0.05$ vs. non targeting). Furthermore, sequential exposure of STC 1 cells to either PTC followed by AHL or AHL followed by PTC showed a reduction of the $[Ca^{2+}]_i$ response to the second application of either PTC or AHL indicating they activate the same signaling pathway.

**Conclusion:** Our results indicate that PTC and AHL activate the same signaling pathway and support our hypothesis that intestinal T2R138 senses bacterial products to mediate a functional response in EEC cells. We hypothesize that the direct or indirect activation of intracellular signal transduction pathways in EEC cells in response to bitter receptor agonists or bacterial products triggers the release of GI peptides that activate enteric or afferent fibers and/or modulate the activity of adjacent or distant target cells.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0901 IMPLICATION OF STREPTOCOCCUS BOVIS IN COLORECTAL CARCINOGENESIS AND OTHER GASTROINTESTINAL PATHOLOGY

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**Introduction:** The association of Streptococcus bovis (SB) endocarditis and colon carcinoma has been reported previously. However the relationship between SB bacteraemia (SBB) and colorectal neoplasia (CRN) or other gastrointestinal conditions is still under controversy and maybe underestimated.

**Aims & Methods: Aims** Determine risk factors SBB-associated and evaluate the association between SBB and CRN and other gastrointestinal conditions. **Methods** Retrospective case-control study of all patients with SBB registered in microbiological system (cases), between 2000–2013. They were compared with asymptomatic subjects with no SBB or personal/familial history of CRN, who underwent screening colonoscopy. Cases were paired with controls for gender and age (±3years) in a proportion of 1:2. Variables evaluated included clinic, laboratorial, pathologic, comorbidities, CRN risk, temporal relation of CRN and SBB diagnosis and mortality.

**Results:** Included 57 patients with SBB (mean age: $72.3 \pm 13.8$vs$71.8 \pm 13.3$yo; $p = 0.825$); male gender: 66.7%vs66.7%; $p = 1.000$). About 74.0%(42/57) of SB were detected in the last 6 years of study. All patients underwent colonic imagiological and/or endoscopic evaluation. An half of patients performed echocardiogram, with endocarditis diagnosis in 25.6%(vs0.0%; OR 1.33; $p < 0.001$), being 28.6% previously diagnosed and 64.3% concomitant to SBB. CRN prevalence was higher in cases (61.4%vs3.5%; OR43.75;$p < 0.001$): 47.4% adenomas with low-grade dysplasia (vs3.5%; OR24.75, $p < 0.001$), 1.8% adenomas with high-grade of dysplasia (vs0.0%; $p = 0.156$) and 12.3% invasive carcinomas (vs0.0%; OR1.14; $p < 0.001$). In case of adenoma diagnosis, 70.0% presented ≥2 adenomas and 18.5%(vs0.0%; OR1.08; $p = 0.004$) with location in the colon right-sided. Relatively to invasive carcinomas, 57.1% were located in sigmoid/rectum. Four cases had concomitant diagnosis to SBB, 5 cases previously ($3.6 \pm 2.3$years) and 5 cases posteriorly ($2.4 \pm 1.7$years). About 77.0% (vs57.0%; $p = 0.010$) had benign gastrointestinal conditions, ≥2 in 45.6% (vs35.1%; $p = 0.183$). Biliary lithiasis (38.6%vs8.8%; OR6.54; $p < 0.001$), splenic infarction (3.5%vs0.0%; OR1.04; $p = 0.044$), liver hemangioma (7.0%vs0.0%; OR1.08; $p = 0.004$), chronic liver disease (14.0%vs1.8%; OR13.39; $p = 0.001$), esophageal varices (8.8%vs1.8%; OR5.39; $p = 0.029$), ischemic colitis/perianal abscess (3.5%vs0.0%; OR1.04; $p = 0.044$) and Clostridium difficile infection (5.3%vs0.0%; OR1.05; $p = 0.013$) were the most common SBB-associated conditions. Other gastrointestinal neoplasia than CRN occurred in 8.8%(vs2.6%; $p = 0.172$) with significate association for pancreatic and hepatocellular carcinomas (3.5%vs0.0%; OR1.04; $p = 0.044$). After multivariate analysis, independent risk factors to SBB were atrial hypertension (59.6%vs22.8%; OR4.61; $p = 0.004$), alcoholism (22.8%vs5.3%; OR10.10; $p = 0.004$), cerebrovascular disease (15.8%vs4.4%; OR4.27; $p = 0.043$), acute myocardial infarction (12.3%vs1.8%; OR7.25; $p = 0.042$), endocarditis (OR1.23; $p = 0.030$), chronic liver disease (OR11.36; $p = 0.028$), kidney dialysis (17.5%vs2.6%; OR12.99; $p = 0.038$) and osteoarthrosis (12.3%vs3.5%; OR6.85; $p = 0.018$). Mortality rate was 45.6%(26/57) with one case related to SB endocarditis. One patient died due to sepsis in early CRN post-operative and no CRN recurrence was registered.

**Conclusion:** SBB prevalence has been increasing. CRN was significant higher in SBB patients, suggesting a major role in colorectal carcinogenesis and an important indicator of occult neoplasia with 60.0% of CRN diagnosed previous or concomitant with SBB. All patients with SBB should perform colonoscopy, even if asymptomatic and a close follow-up in first years after SBB diagnosis. The high association with other benign and malign gastrointestinal conditions suggest the necessity of further investigation beyond colonoscopy or echocardiogram. High mortality seems to be related with multiple comorbidities.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0902 THE ASSOCIATION BETWEEN SMOKING DURATION AND ABSTINENCE WITH ODDS OF COLORECTAL ADENOMAS

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**Introduction:** Colorectal cancer (CRC) is a common and lethal disease, known to develop gradually from its precursors, the most common are adenomatous polyps. Smoking is an established risk factor for colorectal neoplasia but the association with smoking duration and abstinence is yet to be established.

**Aims & Methods:** To evaluate the association between smoking parameters and odds of colorectal adenomas diagnosis in colonoscopy. A case control study among 40–70y patients at low-medium risk for CRC, undergoing screening or alarming symptoms colonsocopy. Cases with colorectal polyps and controls with no current or previous polyps were evaluated for demographic, lifestyle, anthropometric, clinical and metabolic parameters. Severe or GI background illness were exclusion criteria.

**Abstract No: P0903**

**Table:** Characteristics of CRC cases and non-CRC individuals in 2002 and 2014.

| | 2002N = 1,126,644 CRC N = 921 n (%) | Non-CRCN = 1,125,723 n (%) | 2014N = 1,758,198 CRCN = 1330 n (%) | Non-CRCN = 1,756,868 n (%) |
|---|---|---|---|---|
| **Age at start date (years)** | | | | |
| 40–49 | 32 (3.5) | 330,063 (29.3) | 68 (5.1) | 577,167 (32.9) |
| 50–59 | 115 (12.5) | 305,523 (27.1) | 215 (16.2) | 464,427 (26.4) |
| 60–69 | 244 (26.5) | 234,955 (20.9) | 334 (25.1) | 374,036 (21.3) |
| 70–79 | 355 (38.5) | 174,098 (15.5) | 421 (31.7) | 229,621 (13.1) |
| 80–89 | 175 (19.0) | 81,084 (7.2) | 292 (22.0) | 111,617 (6.4) |
| **Sex** | | | | |
| Men | 501 (54.4) | 523,503 (46.5) | 734 (55.2) | 866,071 (49.3) |
| Women | 420 (45.6) | 602,220 (53.5) | 596 (44.8) | 890,797 (50.7) |
| **Morbidities** | | | | |
| Obesity* | 116 (12.6) | 169,036 (15.0) | 360 (27.1) | 441,310 (25.1) |
| Hypertension | 225 (24.4) | 176,647 (15.7) | 435 (32.7) | 339,158 (19.3) |
| Heart failure | 30 (3.3) | 17,086 (1.5) | 30 (2.3) | 16,112 (0.9) |
| Atrial fibrillation | 33 (3.6) | 20,783 (1.8) | 82 (6.2) | 36,865 (2.1) |
| **Medications** | | | | |
| Low-dose aspirin | 150 (16.3) | 113,852 (10.1) | 220 (16.5) | 156,206 (8.9) |
| Proton pump inhibitor | 97 (10.5) | 69,225 (6.1) | 293 (22.0) | 266,005 (15.1) |
| Antihypertensive | 409 (44.4) | 316,728 (28.1) | 722 (54.3) | 519,072 (29.5) |
| Warfarin | 29 (3.1) | 19,844 (1.8) | 84 (6.3) | 37,797 (2.2) |
| **Bowel screening** | 34 (3.7) | 11,472 (1.0) | 190 (14.3) | 187,548 (10.7) |

*Body mass index $\geq$30 kg/m$^2$. CRC, colorectal cancer.

**Results:** Among 724 participants, multivariate analysis revealed that relative to never smokers, smoking (ever) and pack years (PY) were significantly associated with colorectal adenomas (OR = 1.85, 95% 1.35–2.53 and OR = 1.02, 95%CI 1.01–1.03). Relative to current smokers, participants who stopped smoking showed decreased association with adenomas (OR = 0.50, 95%CI 0.31–0.81). Smoking abstinence for more than 5 years before colonoscopy was associated with reduced odds for adenoma (OR = 0.80, 95%CI 0.66–0.97) compared to less than 5 years, and even more so when abstinence duration exceeded 25 years (OR = 0.33, 95%CI 0.16–0.68).
**Conclusion:** These results highlight the need to better define smoking habits in order to predict colorectal neoplasia and recommend appropriate screening. These results call for further validation in additional studies of larger samples.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0903 SECULAR TRENDS IN COLORECTAL CANCER IN THE UNITED KINGDOM

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**Introduction:** Registry data show survival of colorectal cancer (CRC) in the United Kingdom (UK) is poor compared with other European countries and the United States[1], yet these data sources lack information on patient comorbidities and medications used, which could help explain these differences.
**Aims & Methods:** Using The Health Improvement Network primary care database in the UK, we aimed to describe secular trends in CRC incidence and characteristics of CRC cases. Among individuals aged 40–89 years from 2000–2014, we identified first ever cases of CRC and calculated incidence rates (IRs) with 95% confidence intervals (CIs). For all CRC cases and non-cases in two separate calendar years (2002 and 2014), we obtained data on demographics, and characteristics in relation to entry into the study year (start date): body mass index (any time up to start date), morbidities and bowel screening (at start date or within 5 years prior) and current medication use (use 0–30 days prior start date).
**Results:** CRC IRs per 10,000 person-years (pyrs) were relatively constant across the study period; 9.27 in 2000, 10.65 in 2007 and 8.79 in 2014. IRs were higher in men than women, 11.44 versus (vs.) 7.40 per 10,000 pyrs in 2000, and 9.39 vs. 7.38 per 10,000 pyrs in 2014. As shown in the Table, a rise was seen in the proportion of CRC cases diagnosed at <60 years. Prior bowel screening increased in both CRC cases and non-cases. Greater rises in obesity, hypertension, atrial fibrillation and current use of proton pump inhibitors, anti-hypertensives and warfarin, were seen among CRC cases compared with non-cases. Current use of low-dose aspirin remained the same in CRC cases and decreased slightly in non-cases.
**Conclusion:** CRC incidence has remained relatively stable in the UK over the last decade. The increased prevalence of some comorbidities and medication use among CRC cases should be considered when evaluating patterns in CRC survival.
**Disclosure of Interest:** L. Cea Soriano: LCS works for CEIFE, which has received research funding from Bayer Pharma AG
M. Soriano-Gabarró: MS-G is a full-time employee of Bayer Pharma AG, the funder of this study
L.A. García Rodríguez: LAGR works for CEIFE, which has received research funding from Bayer Pharma AG. LAGR has also served as an advisory board member for Bayer Pharma AG

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## P0904 MUCINOUS AND SIGNET-RING CELL COLORECTAL CANCER: RESULTS OF A POPULATION BASED COHORT

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**Introduction:** Most colorectal cancers are classical adenocarcinomas (AC). Less frequent histological subtypes are mucinous adenocarcinomas (MAC) and signet-ring cell carcinomas (SC), which differ from AC in clinicopathology and prognosis. Aim of this study was to define relevant characteristics of mucinous and signet ring cell colorectal cancer on a European population based cohort.
**Aims & Methods:** All newly diagnosed AC, MAC, and SC between 1998 and 2012 within the catchment area of the Munich Cancer Registry were evaluated regarding clinical, histopathological and survival data. The Munich Cancer Registry is a WHO approved population based clinical cancer registry, and member of the International Agency for Research on Cancer (IARC) as well as European Network of Cancer Registries (ENCR), thus warranting thorough data documentation and validation. Cumulative incidence was used to calculate time to locoregional recurrence and distant recurrence.
**Results:** AC occurred in 25,172 patients (90%), MAC in 2,724 (9.7%), and SC in 160 (0.6%). AC were less frequently localized in the proximal colon (34%) compared to MAC (57%, $p < 0.001$) and SC (76%, $p < 0.001$). Both, MAC and SC had higher T, N, and M categories, lymphatic invasion, and worse grading ($p < 0.001$ for each). There were significant differences regarding the 10-year cumulative incidence of locoregional recurrence ($p < 0.001$), and distant recurrence ($p < 0.001$). For AC, the five year overall survival was 59% (95% confidence interval 58.0; 59.3), for MAC 52% (50.2; 54.2), and for SC 40% (32.1; 48.5; $p < 0.001$). However, MAC or SC did not remain independent prognostic factors for overall survival compared to AC upon multivariable analysis ($p = 0.981$).
**Conclusion:** This large European population based cohort of patients with colorectal AC, MAC, and SC shows for the first time different specific histopathological characteristics and recurrence patterns. MAC and SC are diagnosed at more advanced tumor stages and therefore entail reduced survival rates.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0905 INDICATION FOR COLONOSCOPY CORRELATES WITH STAGING AT TIME OF COLORECTAL CANCER DIAGNOSIS

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**Introduction:** **B**urgenland **PRE**vention trial of colorectal cancer **D**isease with **I**mmunologi**C**al **T**esting (B-PREDICT) aims to reduce colorectal cancer (CRC) incidence. All inhabitants of Burgenland aged between 40 and 80 years are included in annual fecal immunochemical test (FIT)-based screening. FIT positive tested individuals were subjected to colonoscopy. Recently, test results of 12 years screening were evaluated to assess the CRC stage in correlation with the indication for colonoscopy.

**Aims & Methods:** B-PREDICT, initiated in 2003 was expanded to the whole province Burgenland in 2006. Annually, more than 150,000 individuals aged between 40 and 80 years are invited to participate in FIT screening. In total, 1,400,000 stool sample containers were delivered to the target group and 547,672 used sample containers were returned, reflecting a participation rate of 39.1%. A qualitative assay was used until 2009, that was replaced by a quantitative system (OC-Sensor, Mast Diagnostica, Germany, cut-off 50 ng hemoglobin/mL) in 2010. In total, 2,160 patients with initial diagnosis (ID) of CRC were recorded during the observation period. 1,301 colonoscopies, performed within 30 days before ID were analyzed to assess the correlation of indication for colonoscopy and staging or tumor size at time of ID.

**Results:** Observed distributions of UICC stage within the different indication groups were: for stage I CRC, 26% screening colonoscopy, 29% positive guaiac test and 38% positive FIT. Pre-testing with FIT was only exceeded by 62% follow-up care after adenoma finding and 88% planned polypectomy. Stage IV CRCs were most frequently diagnosed in the indication suspected malignancy (46%) followed by diarrhea (41%), loss of weight (40%) and abdominal pain (34%) compared to the less frequent indications screening colonoscopy (23%), FIT (11%) and guaiac test (8%). Regarding tumor size, T1 CRC detection rate of indication positive FIT (31%) was only exceeded by the two particular subgroups follow-up care after adenoma (43%) and planned polypectomy (57%). Guaiac test and follow-up after CRC (both 22%) were followed by screening colonoscopy (20%). In symptomatic patients, most T3 colorectal tumors were detected due to anemia (58%), obstipation (50%), abdominal pain (49%), loss of weight (45%), abnormal defecation (41%) and hematochezia (38%).

**Conclusion:** The factor indication for colonoscopy correlates with stage and tumor size at time of ID. Diagnosis of CRC within the subgroup of FIT-triggered colonoscopies is beneficial regarding both, stage and size of tumor.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0906 PATIENT SEX IS ASSOCIATED WITH LYMPH NODE METASTASIS IN T1 COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** About 10% of patients with T1 colorectal cancers have lymph node metastases (LNM), requiring node dissection along with surgical resection. Previously identified risk factors for LNM include lymphovascular invasion, histologic grade, tumor budding and degree of submucosal invasion. Recently, patient sex was also reported to affect the occurrence of LNM.(1)

**Aims & Methods:** The aim was to assess whether patient sex was predictive of LNM in T1 colorectal cancer. We searched public databases, including PubMed, EMBASE and the Cochrane Central Register of Controlled Trials, utilizing keywords related to "T1 colorectal cancer" and "lymph node". All relevant studies reporting the adjusted odds ratio or risk ratio of LNM in relation to patient sex were included. The quality of the studies was classified according to the Quality in Prognosis Studies tool. A random-effects model was used and the quality of the evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach. Meta-analyses were performed using Stata ver. 13.0 (Stata Corp., College Station, TX).

**Results:** The initial database search identified 2,492 publications; of these, 36 studies reported un-adjusted results. Four of the 36 studies reported adjusted results and fulfilled the inclusion criteria for this meta-analysis. Three studies were graded as having a moderate risk of bias, and one had having a low risk of bias. The meta-analysis showed that female sex was related to increased risk of LNM (relative risk 2.45, 95% confidence interval 1.03–3.88). The I-squared statistic was 0.901, classified as very low (+OOO) and was downgraded by the risk of bias, inconsistency and publication bias.

**Conclusion:** Female sex correlated with LNM in patients with T1 colorectal cancer. T1 colorectal cancer in male and female patients might be oncologically different.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0907 CHARACTERIZATION OF PORTUGUESE FAMILIES WITH MUIR-TORRE SYNDROME

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**Introduction:** Muir-Torre syndrome (MTS) is a rare genetic condition with an autosomal dominant inheritance. MTS is the combination of skin tumours (such as sebaceous adenomas (SA), sebaceous carcinomas (SC) and keratoacanthomas (KA)) and visceral malignancy. MTS is considered a subtype of Lynch syndrome (LS), usually associated with MSH2 mutations.

**Aims & Methods:** The aim of this study was to characterize MTS families from a Portuguese centre. Retrospective analysis of 9 consecutive families with MTS followed in a specialized centre between 1997 and 2014. We collected demographic data, tumour types, age at diagnosis and DNA mismatch repair gene mutations.

**Results:** Of 9 families, 8 had MSH2 and one MLH1 pathogenic germline mutations. There were 35 mutation carriers (21 F;14 M) and 71.4% of those developed a total of 61 tumours [mean number of tumours per patient: $2.44 \pm 1.94$ (1–10); mean age: $53.2 \pm 14.3$ years). LS spectrum tumours: colorectal (44%), endometrial (12%), KA (8%), SC (5%), SA (5%), urothelial (3%), stomach (3%), ovarian (2%), small bowel (2%) and brain (2%). We also found tumours not belonging to LS spectrum such as other skin tumours (8%), prostate (3%), breast (2%) and neuroendocrine neoplasias (2%). There were 25 index tumours (mean age: $43.9 \pm 13.2$ years); colorectal was the most frequent (52%), followed by endometrial (16%), KA (8%), SC (4%), urothelial (4%), stomach (4%), ovarian (4%), small bowel (4%) and brain (4%). In 2 cases the index tumour was KA/SC and those patients developed also other neoplasias not associated with LS.

**Conclusion:** The presence of skin tumours such as SA/SC/KA should raise awareness for the diagnosis of MTS, especially because they may present as an index tumour. The identification of MTS families has an important impact in patient management and surveillance strategies.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0908 THE ASSOCIATION OF LOW PENETRANCE VARIANTS IN DNA REPAIR GENES WITH COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** Approximately 35% of colorectal cancers (CRC) are attributable to heritable factors. With only 6% contributed by known hereditary syndromes, the remainder of this risk may be due to lower penetrance variants. Genomic stability relies not only on accurate mechanisms of DNA replication but also on the repair of damage caused by replication errors or the environment. Complex conserved DNA repair pathways have evolved which include Base Excision Repair (BER), Nucleotide Excision Repair (NER), Mismatch Repair (MMR), Reverse Repair (RR) and Double-Strand Break (DSB) repair. It is thought that mutations in DNA repair and replication genes are present in over 58% of cancer cell lines and therefore it is expected that those with DNA repair mutations will be at increased risk of CRC. However the role of low penetrance polymorphisms of DNA repair in CRC risk genes is unclear.

**Aims & Methods: Aim**: To perform a systematic review and meta-analysis to assess the association of DNA repair gene polymorphisms with the risk of CRC. **Methods**: A systematic literature review of the Pubmed and HuGENet databases was conducted and studies were included/excluded based on pre-specified criteria. The per allele model was used to assess the risk attributed to each identified variant, by calculating pooled odds ratios. Heterogeneity was investigated by subgroup analyses for ethnicity and tumour location. Publication bias was investigated using funnel plots and Egger's test. Statistical analysis was conducted using the R program (version 3.2.4).

**Results:** 64 polymorphisms in 26 different DNA repair genes were identified. Meta-analyses were conducted for 22 of these polymorphisms in 17 genes, including between 1706 to 9682 cases per polymorphism. 6 polymorphisms were significantly associated with the risk of colorectal cancer. Subgroup analysis revealed ethnicity was not a source of heterogeneity, however tumour location was significantly associated with OGG1 and CRC risk (Table 1). Egger's test revealed no publication bias.

**Table 1:** Polymorphisms significantly associated with CRC and subgroup analysis for tumour location.

| Pathway | Gene | Polymorphism | Odds Ratio | 95% CI |
|---|---|---|---|---|
| BER | APE1 | rs1130409 | 1.15 | 1.06–1.24 |
| BER | PARP1 | rs1136410 | 1.16 | 1.04–1.30 |
| NER | ERCC5 | rs17655 | 1.11 | 1.05–1.18 |
| NER | XPC | rs2228001 | 1.08 | 1.01–1.15 |
| DSB | RAD18 | rs373572 | 1.32 | 1.16–1.49 |
| RR | MGMT | rs12917 | 0.81 | 0.68–0.98 |
| **Subgroup Analysis for rs1052133** | | | | |
| **Pathway** | **Gene** | **Analysis Type** | **Odds Ratio** | **95% CI** |
| BER | OGG1 | Colon vs Control | 0.93 | 0.81–1.05 |
| | | Rectum vs Control | 1.176 | 1.03–1.34 |
| | | Colon vs Rectum | 0.79 | 0.67–0.92 |
| | | Rectum vs Colon | 1.26 | 1.09–1.47 |

**Conclusion:** The 6 polymorphisms associated with a significant association with CRC risk fell within the BER, NER, RR and DSB repair pathways confirming their importance in CRC risk. Interestingly, no polymorphisms within the MMR pathway were found to be associated with significant risk of CRC in meta-analysis. Advances in the identification of new polymorphisms and genotype technique would allow for more accurate gene analysis. Knowledge of which DNA repair gene polymorphisms have a role in CRC will allow risk assessment and/or treatment to be tailored to suit the needs of each individual patient, affording a more personalised approach to medicine.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0909 DIETARY EMULSIFIERS INDUCED LOW-GRADE INTESTINAL INFLAMMATION FAVORS COLONIC CARCINOGENESIS

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**Introduction:** Colorectal cancer (CRC) is among the most common human malignancies and has been firmly linked to chronic intestinal inflammation, giving rise to the term of "colitis-associated cancer" (CAC). The development of CAC in patients suffering from IBD is one of the best characterized examples of an association between intestinal inflammation and carcinogenesis. Intestinal microbiota is playing an important role in the development of colorectal carcinogenesis, mainly by providing pro-inflammatory signaling that can favor the development of cancer. We recently described that emulsifiers, detergent-like molecules that are a ubiquitous component of processed foods, disrupt mucus-bacterial interactions and induced low-grade inflammation (1).
**Aims & Methods:** Colitis-associated cancer susceptibility was analyzed in mice subjected to a chronic exposure to commonly used emulsifier, carboxymethylcellulose and Polysorbate 80. Tumor burden, proliferation/apoptosis balance, inflammatory marker lipocalin-2 and microbiota pro-inflammatory potential were analyzed.
**Results:** Emulsifier consumption induce low-grade intestinal inflammation, associated with microbiota encroachment, altered species composition and increased pro-inflammatory potential. Those emulsifier-induced perturbation of the microbiota/host relationship promote colonic carcinogenesis, with an increased tumor burden. through a pro-inflammatory environment. Moreover, the altered intestinal microbiota associated with emulsifier consumption was sufficient to drive alterations in some major proliferation and apoptosis pathways.
**Conclusion:** We found here that emulsifier-induced low-grade intestinal inflammation and proliferation/apoptosis balance alteration lead to an exacerbation of AOM/DSS-induced carcinogenesis. These findings support the concept that a perturbed host-microbiota interactions resulting in intestinal inflammation can promote colonic carcinogenesis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0910 15-LIPOXYGENASE METABOLITES IN HUMAN COLON MUCOSA, ADENOMA AND CARCINOMA TISSUES

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**Introduction:** An elevation of prostaglandin E2 (PGE2) level, a product of arachidonic acid (AA, 20:4 n-6) and cyclooxygenases 2 (COX2), is a hallmark in colorectal carcinoma (CRC). While omega-6 polyunsaturated fatty acid (n-6 PUFA) metabolites have mostly pro-inflammatory properties, anti-inflammatory effects are generally attributed to n-3 PUFA metabolites. Recent studies indicated an increase of n-6 PUFA levels and a decrease of n-3 PUFA levels in CRC. Besides, a downregulation of the 15-lipoxygenase (LOX) pathway of the arachidonic acid (AA, 20:4 n-6) cascade has also been described in CRC cells. The role of 15-LOX in the context of carcinogenesis in the colon is still controversial. Several studies postulated tumor suppressing properties of 15-LOX while other investigations suggested pro-inflammatory roles of 15-LOX and its metabolites [1–3]. However, a detailed insight of lipid metabolite changes has not yet been revealed.
**Aims & Methods:** With the help of liquid chromatography-tandem mass spectrometry (LC–MS/MS) we investigated LOX metabolite profile in normal human colon tissue as compared to colorectal carcinoma and adenoma tissue, respectively. After written informed consent according to the declaration of Helsinki, colonoscopy was performed and each patient underwent biopsies of macroscopically intact colon mucosa. In case of adenoma or carcinoma representative tissue biopsies were taken. All samples were immediately quick frozen on dry ice and then stored at −80°C. Lipid metabolite extraction and subsequently quantification by LC-MS/MS was carried out according as described previously [4]. Concentrations of lipid metabolites are expressed in pmol/g tissue.
**Results:** We investigated lipid profile changes in human colorectal carcinoma (n = 9) and adenoma (n = 34) tissue biopsies, focusing on n-6 – and n-3 PUFA metabolites as well as on all known branches of the AA cascade. Human colon adenoma tissue showed significant increased levels of AA derived lipid mediators prostaglandin E2 (PGE2) and 15-hydroxyeicosatetraenoic acid (15-HETE) compared to healthy tissue. Levels of the EPA- derived metabolite 15 - hydroxypentaenoic acid (15-HEPE) and the DHA- derived metabolite 17 hydroxydocosahexaenoic acid (17-HDHA), known as the precursors /pathway indicators of resolvins and protectins, were elevated in adenoma tissue. Human colon carcinoma tissue also showed an increased level of 15-HETE. 15-HEPE and 17-HDHA were also increased in carcinoma tissue.
**Conclusion:** The approach presented here shows the simultaneous quantification of AA, EPA and DHA derived cascade metabolites by liquid chromatography/tandem mass spectrometry and provides a detailed insight into lipid metabolite profile changes from colon tissue to colonic adenoma and carcinoma tissues.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0911 BMI-1 PROMOTES INVASION AND MIGRATION OF COLON CANCER STEM CELLS THROUGH DOWN-REGULATION OF E-CADHERIN

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**Introduction:** Colorectal cancer is the second leading cause of cancer-related mortality in America according to NCCN (National Comprehensive Cancer Network) in 2015(1). It's reported that 15%-25% colorectal patients have had hepatic metastases before diagnosed and over half finally have metastasis. Although the five year survival rate of colon cancer patients after radical surgery is often more than 50%, it drops to less than 10% after metastasis. Cancer stem cell (CSC) is a new theory which appears in recent years about the occurrence, development, metastasis and recurrence of tumors. They are defined as a subpopulation of cancer cells which have the features such as self-renewal, differentiation abilities, metastatic potential, and resistance to conventional chemoradiotherapy (2–4). The discovery of markers of CSCs facilitates the screening and studying of many tumors including the blood, pate, thoracic, abdominal, and genital system cancers. Epithelial mesenchymal transition (EMT) is considered to appear during cancer invasion and migration, or tumor progression. In the process, epithelial cells lose their epithelial

characteristics and adopt mesenchymal appearance or characteristics (5). The down-regulation or loss of E-cadherin, a transmenbrane protein important for cell-cell junction, is treated as the hallmark of EMT (6). The Polycomb group (PcG) of proteins consists of a kind of transcriptional repressors that orchestrate changes in chromatin structure to regulate gene activity (7). Many of PcG proteins are confirmed to alter in human cancers, such as Bmi-1. Bmi-1 was previously known as transcriptional repressor targeting the Ink4a/Arf gene locus; and also described as an oncogene in many solid tumors, playing a critical role in the maintenance of CSCs (8). However, it is rarely reported concerning Bmi-1 and CCSCs at present.

**Aims & Methods:** The aim of this study was to reveal the mechanisms that Bmi-1 promoted invasion and migration of colon cancer stem cells (CCSCs) using colon cancer cell line HCT116. Sphere formation media (SFM) and magnetic cell sorting (MACS) were used to enrich and screen CCSCs. CD133 and CD44 were regarded as markers of CCSCs and they were found to co-express in colon cancer cell line HCT116. Colony formation assay, cell proliferation and viability assays with Cell Counting Kit-8 (CCK8), and nude mice transplantation tumor assay were used to identify CCSCs.

**Results:** $CD133^{+}CD44^{+}$ HCT116 cells showed higher cloning efficiency, greater proliferation ability and viability, and stronger tumorigenicity; thus acting as CCSCs for subsequent studies. In addition, the invasion and migration abilities of $CD133^{+}CD44^{+}$ HCT116 cells obviously decreased when Bmi-1 was silenced by small interfering RNA (siRNA). RT-PCR and Western Blot analysis suggested Bmi-1 impacted negatively on E-cadherin.

**Conclusion:** In summary, Bmi-1 promoted invasion and migration of CCSCs through down-regulation of E-cadherin, probably by inducing EMT. This may offer a new target for cancer therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0913 ASSOCIATION OF COLORECTAL ADENOMA WITH METABOLIC SYNDROME


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**Introduction:** Colorectal cancer and metabolic syndrome shared several risks like obesity, lack of physical activity, and insulin resistance, but the association between these two disease is still unclear.

**Aims & Methods:** The objective of this study was to assess the association of colorectal adenoma with metabolic syndrome (MS). We retrospectively study 289 participants who underwent screening colonoscopy in the University of Hong Kong – Shenzhen hospital from January 2014 to June 2015. The Associations between smoking, drinking, physical activity, aspirin taking, BMI, waist circumference, MS, blood pressure, free blood glucose (FBG), triglyceride (TG), cholesterol (CHOL), high-density lipoprotein (HDL) and colorectal adenoma were evaluated.

**Results:** 159 participants were recruited in adenoma group (AG) and 130 participants in normal group (NG). AG had a bigger body mass index (BMI) [$(23.5 \pm 3.19)$ versus $(22.7 \pm 2.83)$,$P = 0.05$], bigger waist circumference [$(83.4 \pm 10.3)$ versus $(79.6 \pm 13.)$,$P = 0.015$], higher serum HDL level (mmol/L) [$(1.31 \pm 0.286)$ versus $(1.23 \pm 0.271)$,$P = 0.044$], and higher serum CHOL level (mmol/L) [$(5.4 \pm 0.986)$ versus $(5.04 \pm 1.14)$,$P = 0.018$] than NG. No significant differences were existed when comparing hip circumference and waist-hip ratio, as well as serum FBG and TG. The rate of MS in AG is higher than NG (23.3% versus 12.3%,$P = 0.017$), as well as comparing rate of overweight or obesity (35.2% versus 23.1%,$P = 0.025$), hypertension (23.8% versus 14.3%,$P = 0.046$) and hypercholesteremia (40.3% versus 24.6%,$P = 0.017$). But no significant difference were existed in comparison of hyperglycemia, hypertriglyceridaemia or abnormal serum HDL ($P > 0.05$).

**Conclusion:** Metabolic Syndrome increases the risk of having colorectal adenoma. The mechanism may be related to higher serum CHOL and HDL, and causing elevated catabolism of cholesterol. Screening colonoscopy should be enhanced for people diagnosed of MS, especially having central obesity and hypercholesterolemia, to early diagnose and treat colorectal adenoma and prevent colorectal cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0914 PREVALENCE AND CHARACTERISTICS OF UNEXPECTED RECTAL CANCER IN BENIGN APPEARING LARGE NON-PEDUNCULATED RECTAL POLYPS


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**Introduction:** Transanal endoscopic microsurgery (TEM) and endoscopic mucosal resection (EMR) are the most common resection techniques for large non-pedunculated rectal polyps. Despite thorough preoperative endoscopic investigation, unexpected rectal cancer is occasionally encountered at pathological examination of the resected specimen. Little is known about the prevalence and characteristics of unexpected cancer in those lesions that appear benign. This study describes the prevalence of unexpected rectal cancers, the lesion and procedural characteristics and its subsequent treatment and recurrence rates.

**Aims & Methods:** Patients included in this post-hoc analysis were selected from a multicentre randomized controlled trial (TREND study) investigating the recurrence of neoplasia after treatment of rectal polyps with either EMR or TEM between 2009–2013. Patients with a non-pedunculated rectal polyp of $\geq$ 3 cm located between 1–15 cm from the anal verge without endoscopic suspicion of invasive growth, were eligible. If histopathology of the resected specimen revealed invasive growth, patients were excluded from the TREND study and included in this analysis. Data concerning patient, lesion and procedural characteristics as well as additional therapy and surveillance were collected.

**Results:** Unexpected rectal cancer was found in 27/204 included patients in the TREND study (13%); 15 were initially treated with EMR and 12 with TEM. The majority consisted of a T1 cancer ($n = 22$, 81.5%) but also 3 T2 (11.1%) and 2 T3 cancers (7.4%) were detected. The mean lesion size was $47 \pm 11.6$ mm, 18 (78.3%) cancers were moderately to well differentiated and lymphatic or vascular invasion was not detected. Patient and lesion characteristics were similar either between the resection techniques or between malignant and benign lesions included in the TREND study. Resection procedures of malignant lesions were more often assessed as being irradical compared to benign lesions (25.0% vs 8.5%, OR 3.60 (95% CI 1.32–9.84), $p = 0.02$). The success of submucosal lifting during EMR was also lower (60.0% vs 93.1%, $p < 0.001$). Patients initially treated

with EMR received completion surgery in 80.0%, which consisted in 50% of TME (66.7% LAR, 33.3% APR) and in 50% of TEM. Five patients (41.7%) initially treated with TEM received completion surgery, which was according to the TME principle (20% LAR, 80% APR) in all patients. After a mean follow up of 4.4 ± 1.2 years, all patients were alive and one malignant recurrence was detected. Distant metastases were found in 3 patients (11%), whom all underwent surveillance after treating a T1Sm3 carcinoma with TEM.
**Conclusion:** Despite careful lesion assessment, unexpected cancers were encountered in 13% of patients treated for large non-pedunculated rectal polyps. This might impact the strategy how to treat these polyps in the future, since incomplete procedural resection and non-lifting sign during EMR occurred more often in the cancers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0915 CLINICOPATHOLOGIC AND ENDOSCOPIC FEATURES OF EARLY STAGE COLORECTAL SERRATED ADENOCARCINOMA

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**Introduction:** Serrated adenocarcinoma (SAC) is considered to be one of several end-points of the serrated neoplasia pathway. Recently, SAC has been described as distinct variant of colorectal carcinomas, accounting for approximately 7.5% of all advanced colorectal carcinomas, and it has been well known to have a worse prognosis than conventional carcinoma. However, there are no reports about the clinicopathologic features in the early stage of SACs.
**Aims & Methods:** The aim of this study was to clarify clinicopathologic and endoscopic differences in early stage SACs. A total of 40 consecutive SACs in 40 patients at Hiroshima University Hospital during the period from January 2009 until January 2016 were enrolled. The histologic diagnosis of SAC was decided according to the World Health Organization (WHO) classification. In this study, we defined more than 5% of serrated morphology in the cancerous area as SAC, and classified 2 groups as SAC with all serrated morphology (Group A, n = 17) and SAC with non-serrated morphology (Group B, n = 23) in the cancerous area. We examined the clinicopathologic characteristics between 2 groups as follows: gender, age, location (proximal colon/ distal colon/ rectum), tumor size, invasion depth (Tis, T1a, T1b). We also examined the endoscopic findings between 2 groups as follows; tumor surface color (same as normal mucosa, white, red), macroscopic type (protruded, superficial), pinecone-like findings, varicose microvecicular, pit pattern, and NBI magnifying finding (JNET classification, Dig Endosc 2016) at the cancerous area. We also classified the serrated components close to carcinoma into 4 types; sessile serrated adenoma (SSA type), traditional serrated adenoma (TSA type), unclassified type, and non-serrated component type.
**Results:** In clinicopathologic characteristics, there were significantly differences in average tumor size (Group A 27.6 mm vs. Group B 43.1 mm), incidence of T1 carcinoma (Group A 71% vs. Group B 13%), the incidence of tumor color of same as normal mucosa (Group A 47% vs. Group B 17%) between 2 groups ($p < 0.01$). Depth (Tis/T1a/T1b) of SACs was shown in Group A (5/1/11) and Group B (20/1/2), respectively. In SACs smaller than 10 mm, there were no submucosal invasive SACs. However, in SACs larger than 20 mm, the incidence of T1 carcinoma in Group A (70%) was significantly higher than that in Group B (13%) ($p < 0.05$). There were no significant differences in gender, age, location, between 2 groups. In endoscopic findings, there were significant differences in JNET Type 3 (Group A 18% vs. Group B 0%, $p < 0.01$), type V pit pattern (Group A 70% vs. Group B 39%, $p < 0.01$) between 2 groups. There were no significant differences in macroscopic type, pinecone-like findings, varicose microvecicular between 2 groups. Average tumor size of TSA type (42.6 mm) was significantly larger than SSA type (17.2 mm) or non-serrated component type (18.3 mm). SACs with SSA type located in the proximal colon in all cases. The incidence of submucosal invasion of SSA type (80%), Unclassified type (100%) and Non-serrated component type (100%) was significantly higher than that of TSA type (11%).
**Conclusion:** Serrated morphology in the cancerous area and background of non-TSA components indicated the aggressive behavior in early stage SACs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0916 DIAGNOSTIC ACCURACY OF FECAL IMMUNOCHEMICAL TEST IN PATIENTS AT HIGH-RISK FOR COLORECTAL CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** Fecal immunochemical test (FIT) is an alternative screening procedure for individuals in average risk for colorectal cancer (CRC), with increased adherence, safety and low cost. However, evidence on performance of FIT in high-risk population is inconsistent. Thus, we performed a systematic review and meta-analysis to assess the diagnostic accuracy of FIT for CRC and advanced neoplasia (AN: CRC or advanced adenomas) in asymptomatic high-risk population.
**Aims & Methods:** We systematically searched MEDLINE, EMBASE, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, Cochrane Library and grey literature sources through February 2016. We included diagnostic studies that assessed the accuracy of FIT for CRC in patients with family history of CRC or personal history of colorectal cancer or advanced adenoma. We accepted studies that utilized colonoscopy or longitudinal follow-up as reference standard. Quality of the studies was assessed using the QUADAS-2 tool.
**Results:** Thirteen studies with 6250 participants assessed the diagnostic accuracy of FIT for AN, while eight of those (4840 patients) provided data specifically for CRC. Nine studies evaluated quantitative FITs, while only four evaluated a qualitative FIT. Only five studies were deemed at low risk of bias. FIT sensitivity for CRC ranged from 0.25 to 1.00 (median 0.84) and specificity from 0.76 to 0.95 (median 0.89). Due to substantial heterogeneity, we synthesized diagnostic accuracy by means of hierarchical summary ROC (HSROC) model, and calculated summary estimates only for subgroups that used the same cutoffs. In studies using cut off values less than 15$\mu$gHb/g feces FIT pooled sensitivity was 97% (95% CI 71 to 100), specificity 91% (95% CI 90 to 92), positive likelihood ratio 10.6 (95% CI 8.9 to 12.5) and negative likelihood ratio 0.03 (95% CI 0.00 to 0.40). In four studies using cut off values 15 to 25$\mu$g/g pooled sensitivity was 93% (95% CI 73 to 99), specificity 94% (95% CI 91 to 96) positive likelihood ratio 15.1 (95% CI 9.5 to 23.9) and negative likelihood ratio 0.07 (95% CI 0.02 to 0.32). Finally, we calculated respective diagnostic accuracy summary estimates for AN (Table 1).

**Table 1:** FIT diagnostic accuracy for advanced neoplasia (colorectal cancer or advanced adenomas) in asymptomatic patients at high-risk.

| | Cut-off used for advanced neoplasia ($\mu$g Hb/g feces) $< 15$ | $15 \leq x \leq 25$ |
|---|---|---|
| Number of studies | 8 | 5 |
| Number of participants | 3959 | 2712 |
| Sensitivity (95% CI) | 60 (39 to 78) | 42 (32 to 54) |
| Specificity (95% CI) | 92 (90 to 94) | 97 (95 to 98) |
| Positive likelihood ratio (95% CI) | 7.9 (5.4 to 11.5) | 13.1 (9.2 to 18.6) |
| Negative likelihood ratio (95% CI) | 0.43 (0.26 to 0.72) | 0.60 (0.50 to 0.72) |

**Conclusion:** FIT has high overall diagnostic accuracy and can be used in patients at high risk for colorectal neoplasia for establishing the diagnosis of colorectal cancer or advanced neoplasia. Nevertheless, it can only rule out colorectal cancer, at either one of the cut-offs assessed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0917 DIMETHYLARGININE SERUM CONCENTRATIONS EFFECTIVELY IDENTIFY SUBJECTS WITH COLORECTAL CARCINOMA

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**Introduction:** Along the progression from normal colonic mucosa to colorectal cancer systemic metabolic pathways may be affected. We aimed to identify metabolic features and possible biomarkers of colorectal carcinoma and advanced adenoma.
**Aims & Methods:** According to the results of screening colonoscopy 399 patients were allocated to one of 3 groups: colorectal carcinoma (CRC, n = 47), advanced adenoma (AA, n = 55), control (CTRL, n = 297). The serum metabolite profile of all subjects was obtained by API 4000 triple quadrupole mass spectrometer (ABSciex) using the AbsoluteIDQTM p180 kit (BIOCRATES Life Sciences). Significant differences in metabolomics analyses

were determined by Significance Analysis of Microarrays (SAM) using false discovery rate (FDR).
**Results:** The metabolite profile of CRC was markedly different from the other two groups while AA und CTRL were found to largely overlap. In particular, CRC showed significantly higher levels of total dimethylarginine (TDMA), spermine, acyl carnitines C16, C16-OH, sphingomyelin (SM) C22:3 and SM C20:2 (adjusted $p < 0.001$). For differentiation between CRC and subjects without carcinoma biomarker analysis based on Receiver Operating Characteristic (ROC) was conducted. For TDMA an area under the curve (AUC) of 0.923 was found. After exclusion of 18 subjects with eGFR $<60$ ml/min as a potential confounder of TDMA serum concentrations an AUC of 0.934 (95% CI: 0.897–0.970) was calculated. Apart from TDMA, the other above mentioned metabolites showed an AUC of 0.926. Combining all of the most significant, in particular TDMA, spermine, SM 22:3, SM 20:2, C16 and C16-OH, an AUC of 0.955 was obtained for distinguishing CRC from AA or CTRL group members.
**Conclusion:** TDMA serum concentrations may serve as a potential biomarker for the identification of colorectal carcinoma. Its role in colon carcinogenesis needs to be investigated further.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0918 GAS CHROMATOGRAPHY SENSOR PLATFORM FOR DIAGNOSING COLONIC NEOPLASIA USING FAECAL SAMPLES

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**Introduction:** Colorectal cancer (CRC) remains a leading cause of mortality and morbidity worldwide. The incidence has increased by 6% in the last decade and it is the third most common malignancy in the UK, accounting for approximately 15,000 deaths annually, with a 50–55% 5-year mortality rate[1]. Data from the UK Bowel Cancer Screening Programme (BCSP) has clearly demonstrated that detection of CRC at an earlier stage and identification of advanced pre-malignant adenomas can reduce future cancer-associated mortality and morbidity. Currently the BCSP utilises stool-based markers (gFOBt) as a pre-screen prior to colonoscopy which has a sensitivity of 54% and specificity of 80%[2]. Here we propose a platform for the diagnosis of colonic neoplasia.
**Aims & Methods:** Stool was collected from symptomatic patients and those within the BCSP due to undergo colonoscopy. Subsequent outcomes were classified as no-neoplasia, adenoma, cancer and higher-risk adenoma (individual lesion $>1$ cm). The platform is composed of a gas chromatography coupled to a metal oxide gas sensor (OdoReader) and a computer algorithm. The OdoReader separates the volatile organic compounds (VOCs) present in faecal samples, while the computer algorithm identifies resistance patterns associated with specific medical conditions and builds mathematical models to classify unknown samples.
**Results:** A total of 161 faecal samples were analysed, of these 78 had no neoplasia, 18 cancer, 67 at least 1 adenomatous polyp of any size and 18 had higher risk adenomatous disease.

**Table 1:** Results of the repeated double cross-validation applied to faeces samples.

| Comparison | Mean accuracy (%) | Median accuracy (%) | Mean sensitivity (%) | Median sensitivity (%) | Mean specificity (%) | Median specificity (%) |
|---|---|---|---|---|---|---|
| No neoplasia v Adenoma | 72.32 | 71.42 | 72.87 | 71.42 | 71.76 | 71.42 |
| No neoplasia v Cancer | 78.38 | 83.33 | 80.61 | 75 | 76 | 66.66 |
| No neoplasia v Higher risk adenoma | 86.3 | 87.5 | 84.6 | 100 | 88 | 100 |
| High risk adenoma v cancer | 93.36 | 100 | 97.38 | 100 | 89.33 | 100 |

**Conclusion:** This is the first description of an investigation for the positive diagnosis of colonic neoplasia using this methodology. The platform presented here classified samples with accuracies up to 93%. These schemes provide an estimate of out-of-sample predictive accuracy for similar populations. Therefore, the results reported here indicate a successful differentiation of neoplastic and non-neoplastic disease which are superior to FOBt.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0919 USE OF CT COLONOGRAPHY (CTC) IN SELECTED PATIENTS REFERRED ON A SUSPECTED COLORECTAL CANCER PATHWAY TO A UK UNIVERSITY TEACHING HOSPITAL – ASSESSING THE POTENTIAL FINANCIAL BENEFITS OF A STRAIGHT TO TEST MODEL

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**Introduction:** Demands on endoscopy units are rising, with particular pressure coming from changes in the NICE guidance[1] lowering the threshold for suspicion of cancer. Colonoscopy effectively excludes colorectal cancer as a cause for a patient's symptoms but may result in cross-sectional imaging further along the diagnostic pathway and CT colonography (CTC) may address both issues. We propose to pilot a straight to test (STT) model where patients 75 years and over undergo CTC as routine, and assessed the potential financial benefit of this in a UK university teaching hospital.
**Aims & Methods:** Data from 2-week wait referrals for suspected colorectal cancer to UCLH between June 12th 2014 to November 17th 2014 was analysed retrospectively from hospital systems. Data was collected from the time of referral until discharge from the pathway. Using the NHS tariffs (to nearest £) for each investigation/procedure, we calculated the potential financial benefit by directly comparing actual costs incurred versus the potential costs using the STT model.
**Results:** In total, 505 patients were referred, with 477 of these patients sent for further tests; 353 referred for endoscopy (332 colonoscopy), and 110 referred for CTC. The average age of patients for endoscopy was 59.3 years versus 71 years for CTC. In the endoscopy group, 46 patients were aged 75 or older (13%). Table 1 details the costs incurred (excluding staging CT).

**Table 1:** Patients 75 or older who had lower GI endoscopy

| Investigation/Procedure (Tariff in £) | No of patients | Total Cost (£) |
|---|---|---|
| Colonoscopy (433) | 31 | 13423 |
| Colonoscopy + biopsy (465) | 4 | 1860 |
| Therapeutic colonoscopy (469) | 10 | 4690 |
| Flexible sigmoidoscopy (309) | 1 | 309 |
| CTC post endoscopy (238) | 3 | 714 |
| CT abdomen/pelvis (A/P) post endoscopy (137) | 3 | 411 |
| CT Chest/A/P post endoscopy (135) | 1 | 135 |
| | | Total = 21542 |

Had all 46 patients had a CTC initially, this would have resulted in a cost of £10948 and follow-up costs for endoscopy would have been as per further procedures as in Table 1 (£1860 + £4690 + £309), resulting in a total of £17807. In the 5-month period analysed, a potential saving of £3735 (i.e. £21542 − £17807) using the STT model, representing a potential annual saving of £8964.
**Conclusion:** The data demonstrates that potentially ≈ £9000 per annum could be saved by using a STT model to CTC for patients aged 75 years or over in the suspected colorectal cancer pathway. This also would have eased pressure on endoscopy capacity, by diverting patients to excess radiology capacity. Additional factors that could further increase financial savings include careful referral to endoscopy after CTC[2] and stricter adherence to guidelines regarding polypectomy after CTC[3]. These could yield a greater financial benefit as a result of lower conversion rates to endoscopy and associated costs. CTC also offers extra-colonic organ review and may reduce the need for further imaging to explain the patients' symptoms, and account for the 13% in our analysis who required a CT post endoscopy. In our analysis, approximately one-third of patients are estimated to require an endoscopy procedure after CTC in the STT model. Although having two procedures rather than one potentially increases patient distress and inconvenience, it does allow targeted therapeutic colonoscopy, potentially on the same day as the CTC. STT has been demonstrated to reduce outpatient clinic appointments[4], thereby reducing costs which were not analysed in this patient cohort. It does, however, require a trained nurse to screen referrals and discuss the investigation with patients by telephone. Obviously this incurs some expenditure but is associated with greater patient satisfaction[4]. We have embarked on a trial of this novel STT pathway and look forward to presenting the results in the future.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0920 FIT IS A BETTER MARKER FOR COLONIC NEOPLASIA THAN LOWER GI BLEEDING

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**Introduction:** Data regarding diagnostic yield of colonoscopies according to Positive Fecal Inmunochemical Test (FIT) and Rectal Bleeding after excluding anal pathology by external inspection (RB) are scarced.

**Aims & Methods:** Aim. To compare the diagnostic yield of neoplasia when colonoscopy is performed after a positive FIT and in the evaluation of RB. Patients and methods. Retrospective study of colonoscopies performed: 1) within a screening program after positive FIT (Sentinel Gold test) result, 2) as diagnostic evaluation in symptomatic patients (non-screening group) after positive FIT result and 3) due to rectal bleeding after excluding anal pathology. The study was performed between January 1st 2014 and June 30th 2015 in Hospital Clínico Universitario Lozano Blesa, Zaragoza (Spain). Age and sex-adjusted Odds Ratios were calculated by logistic regression analysis.

**Results:** A total of 1.387 colonoscopies (54.1% men) were performed; 524 (37.8%) in colon cancer screening program, 507 (36.6%) due to RB and 356 for diagnostic evaluation after Positive FIT. There were more men in screening group (61.5%) than in the other 2 groups: 48.6% in RB and 50.3% in FIT non-screening group ($p < 0.001$). In 640 (53.9%) colonoscopies neoplasia (adenoma or carcinoma) was found. Neoplasia was more frequent in screening colonoscopies (61.1%) than in those performed by diagnostic evaluation (47.2%) or RB (30%) ($p < 0.001$); (OR = 1.7 IC 95% = 1.3–2.3)($p = 0.002$) compared to FIT in non-screening group; (OR = 2.8, IC95% = 2.1–3.7)($p = 0.000$) compared to RB group. Adenoma was found in 600 (43.3%) colonoscopies and was more frequent in screening colonoscopies (60.1%) than in those performed by diagnostic evaluation (42.1%) or RB (26.6%) ($p < 0.001$); (OR = 2.0 IC 95% = 1.5–2.7)($p = 0.002$) compared to non-screening group and (OR = 3.3 IC95% = 2.5–4.4)($p = 0.000$) compared to RB group. Advanced neoplasia (carcinoma or advanced adenoma) was found in 181 (13%) colonoscopies and was more frequent either in screening colonoscopies (16.4%) or in those performed by diagnostic evaluation (15.4%) than in RB (7.9%) ($p < 0.001$), with no differences between screening and diagnostic group; (OR = 1.7 IC 95% = 1.2–2.6)($p = 0.008$) compared to non-screening group and (OR = 1.6, IC95% = 1.0–2.5)($p = 0.046$) compared to RB group. Carcinoma was found in 89 (6.4%) colonoscopies: 33 (6.3%) in screening group, 34 (9.6%) in those performed by diagnostic evaluation and 22 (4.3%) in RB (p NS). In screening group 78.8% of them were diagnosed in early stages (I or II), compared to 58.8% in diagnostic evaluation and 54.5% in RB (p NS).

**Conclusion:** The yield of neoplasia is low when colonoscopy is performed due to RB. Neoplasia rates found in colonoscopies after a positive FIT are higher than in colonoscopies performed because of RB. FIT is a reasonable option in the diagnostic evaluation of patients prior to colonoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0921 ANALYSIS OF COLORECTAL CANCERS (CRCS) DEPENDING ON THE SCREENING HISTORY FOR CRC SCREENING IN IBARAKI, JAPAN

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**Introduction:** In Japan, colorectal cancer (CRC) screening was launched as a national policy for both sexes aged over 40 years in 1992. As a screening tool, 2-day FIT has been widely accepted.

**Aims & Methods:** The objective of this study is to verify the CRC screening by 2-day FIT with cut-off value of 20$\mu$g hemoglobin/g stool and by comparing the screening history. 2,709 cases, who were detected between 2001 and 2013, were analyzed by screening history, age, locations, sizes, and Dukes group.

**Results:** 1,058(39.1%) cases were detected by the first time screening group and 1,651(60.9%) cases were detected by the repeated screening group. In the first-time group, 823(77.8%) cases were between 50 and 74 years old, and 1,211(73.3%) cases were between 50 and 74 years old in the repeated group. The proportion of cases with the age of 50–74-year-old was significantly higher in the first time group than in the repeated group. With regard to the locations of CRCs, in the first-time group, 309 cases were in the rectum (R), 390 cases were in the sigmoid colon(S), 58 cases were in the descending colon (D), 89 cases were in the transverse colon (T), and 160 cases were in the ascending colon (A/C). In the repeated group, 459 cases were in R, 462 cases were in S, 64 cases were in D, 191 cases were in T, and 411 cases were in A/C. The proportion of D+T+A/C was significantly higher in the repeated group than in the first time group. 992 cases in the first time group and 1,538 cases in the repeated group were reported for sizes. In the first-time group, 586 cases were 1–24 mm, 291 cases were 25–49 mm, and 115 cases were over 50 mm. In the repeated group, 1,040 cases were 1–24 mm, 396 cases were 25–49 mm, and 102 cases were over 50 mm. The size of detected cancers by the repeated group was significantly smaller than by the first time group. In the first-time group, 455 cases were intra-mucosal Dukes A, 281 cases were Dukes A, 137 cases were Dukes B, 139 cases were Dukes C, and 34 cases were Dukes D. In the repeated group, 831 cases were intra-mucosal Dukes A, 444 cases were Dukes A, 137 cases were Dukes B, 139 cases were Dukes C, and 30 cases were Dukes D. The proportion of intra-mucosal Dukes A was significantly higher by the repeated group than by the first time group.

**Conclusion:** Repeated FIT screening might be more efficient to detect CRCs in the proximal colon, smaller CRCs, and CRCs of intra-mucosal Dukes A.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Table P0921**

| | Locations | | | | | |
|---|---|---|---|---|---|---|
| | R | S | D | T | A/C | Unknown |
| First time group | 309 (29.2%) | 390 (36.9%) | 58 (5.5%) | 89 (8.4%) | 160 (15.1%) | 52 (4.9%) |
| Repeated group | 459 (27.8%) | 462 (28.0%) | 64 (3.9%) | 191 (11.6%) | 411 (24.9%) | 64 (3.9%) |
| P value | 0.4207 | 0.0000 | 0.0493 | 0.0085 | 0.0000 | 0.1927 |
| | Sizes | | | | | |
| | 1 - 24mm | 25–49 mm | 50 mm- | | | |
| First time group | 586 (59.1%) | 291 (29.3%) | 115 (11.6%) | | | |
| Repeated group | 436 (67.6%) | 255 (25.7%) | 102 (6.6%) | | | |
| P value | 0.0000 | 0.0476 | 0.0000 | | | |
| | Dukes | | | | | |
| | Intra-mucosal A | A | B | C | D | Unknown |
| First time group | 455 (43.0%) | 281 (26.6%) | 146 (8.8%) | 174 (10.5%) | 34 (2.1%) | 22 (1.3%) |
| Repeated group | 831 (50.0%) | 444 (26.9%) | 137 (12.9%) | 139 (13.1%) | 30 (2.8%) | 16 (1.5%) |
| P value | 0.0002 | 0.8484 | 0.0007 | 0.0390 | 0.1944 | 0.6979 |

## P0922 USEFULNESS OF PET-CT FOR DETECTING THE PREMALIGNANT LESIONS IN COLON

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**Introduction:** The utilization of positron emission tomography (PET) with computed tomography (CT) has increased exponentially, with increment of cancer and health examination. As an increasing number of unexpected incidental FDG uptake are reported, detection of colonic premalignant lesions besides colon cancer accidently is increased. The aim of this study was to assess the usefulness of PET-CT to detect colonic premalignant lesions, especially colonic advanced adenoma (villous or >10 mm adenomas, high grade dysplasia).

**Aims & Methods:** We retrospectively analyzed the records of 1,011 consecutive patients (1,233 pairs of examinations), who underwent an FDG PET-CT scan and colonoscopy simultaneously within a 1-year interval for various reasons at our center. We did not make clear the order of the incident and excluded the cases in which polyps were removed the lesions by polypectomy or biopsy before PET-CT and the interval between the two examinations exceeded a 1 year. Accuracy and predictive value of PET-CT were analyzed in all polyps and in advanced groups respectively.

**Results:** We included 996 pairs of examinations (excluded cases: 105 previous polypectomy, 102 > 1year interval, 30 no pathologic confirmation). We found that 99 foci revealed meaningful lesions on the same sites in both PET-CT and colonoscopy. The positive and negative predictive values of PET-CT to detect colonoscopic abnormalities were 81.8% (99/121) and 58% (508/875) respectively. The sensitivity and specificity of PET-CT for overall adenoma was 21% and 95.8% each. Moreover, the sensitivity of PET-CT for advanced adenomas was 85% (68/80). The rate of false positive was 4% (22/530) and the lesions were often related to physiologic uptake such as bowel retention and inflammation. The false negative results represented 78.8% (367/466) when there were the lesions on same site in both PET-CT and colonoscopy. Tubular adenoma with low-grade dysplasia was most frequent finding (19.2%). A difference in the mean SUVmax between false-positive (6.2) and true-positive colonic FDG foci (8.2) was statistically significant ($p < 0.01$).
**Conclusion:** PET-CT revealed relatively high positive predictive value and negative predictive value. Especially, the sensitivity for advanced adenomas (85%) was higher than overall sensitivity (21%). However, PET-CT does not seem sensitive tool for colonic premalignant lesions because of the rate of false negative results (78.7%). Nevertheless, the sensitivity for advanced adenomas was significantly high. Thus, we should pay particular attention to detect the lesions detected by PET-CT of high-intensity focal FDG uptake through colonoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0923 A NEW BLOOD TEST FOR THE DETECTION OF COLORECTAL CANCER (CRC): MEASUREMENT OF NATURAL KILLER CELL ACTIVITY (NKA) IN PATIENTS UNDERGOING COLONOSCOPY


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**Introduction:** A large number of studies on several cancers (prostate, colon, breast, lung, and others) have been published confirming that patients with cancer have lower NKA compared to healthy control subjects. Low NKA has been linked to a higher risk of cancer and has been reported in CRC patients, with lower activity associated with metastatic disease. The cancer-associated drop in NKA has been demonstrated, either using the Research Use Only Cytotoxicity Assays ($^{51}$Cr cytotoxicity gold standard assay or immunofluorescence assay) or more recently using a novel simple blood test, a commercially available in vitro diagnostic device (IVDD) which measure NKA in a small volume of whole blood (Koo et al, 2013;Lee et al, 2014).
**Aims & Methods:** The aim of this study is to evaluate the sensitivity, specificity, positive and negative predictive values of the IVDD in patients with CRC and adenomatous polyps (AP) Method: The current study measured NKA with a new commercially available blood test in 869 consecutive subjects presenting for screening of CRC or prescribed colonoscopies. Blood was drawn on the day of colonoscopy prior to the procedure and the biological assay performed as per the manufacturer's directions.
**Results:** In the 762 evaluable subjects, statistically significant differences were found between the NKA of patients positive for CRC (n = 21), confirmed by colonoscopy and pathological verification, and that of patients negative for CRC (n = 741) (CRC mean 344.2 pg/mL (SD:881.7), CRC-negative mean 731.5 pg/mL (SD:1019.3), p = 0.001; CRC median 87.0 pg/mL (IQR:49.0–151.0), CRC-negative median 294.8 pg/mL (IQR: 98.7–895.5), $p \leq 0.001$). In this population, the prevalence was 2.8% for CRC and 13.4% for AP≥10 mm. Receiver Operator Characteristics (ROC) analysis of the data show that the optimum cut-off for detection of CRC is 181.3 pg/mL, with an area under the curve of 71%. At a cut-off of 200 pg/mL, sensitivity of the IVDD for detection of CRC was 85.7%, with a specificity of 59.6%, positive and negative predictive values of 5.7% and 99.3% respectively (see Table 1). At a cut-off of 500 pg/mL, statistical analysis of the IVDD for detection of AP10 mm (n = 102) showed a sensitivity of 56.9%, a specificity of 35.0%, positive and negative predictive values of 11.9% and 84.0% respectively. Results of NKA and Colonoscopy Findings.
**Conclusion:** The present study using a new simple blood test confirms that the measurement of NKA may be a useful tool in clinical practice to assess the risk of CRC. This blood test, which demonstrated high sensitivity and negative predictive value for CRC, could be a valuable new tool for the detection of CRC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0924 PRIMARY TUMOR RESECTION IN METASTASIZED COLORECTAL CANCER – A META-ANALYSIS


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**Introduction:** Approximately 20% of all patients with colorectal cancer present with distant metastases at the time of diagnosis. During the last years, whenever feasible, complete resection (R0) of the primary tumor as well as of all metastases has been propagated because of substantially improved survival rates for this approach. However, the prognostic role of resection of the primary tumor remains a matter of debate in the case of non-resectable multiple metastases. This meta-analysis evaluates the current literature regarding the risks and benefits of palliative resection of the primary colorectal cancer in the metastasized setting.
**Aims & Methods:** A Medline/PubMed search was performed in March 2016 in order to identify original studies that compare asymptomatic stage IV colorectal cancer patients who were treated with primary tumor resection (with or without systemic or palliative intended antitumoral therapy) versus patients who were treated without primary tumor resection (with or without systemic or palliative intended antitumoral therapy; with or without palliative surgical procedures other than tumor resection). The identified studies were analyzed according to the PRISMA statement. Baseline characteristics as well as morbidity, mortality and overall survival for the two groups were compared.
**Results:** Of 37,413 screened articles, finally 56 studies with a total of 148,151 patients met the inclusion criteria. All articles were retrospective reports. 94,456 patients underwent palliative primary tumor resection and 53,695 received non-surgical therapy of the primary tumor. Primary tumors of the colon were significantly more often resected than primary tumors of the rectum (71% versus 49%, $p < 0.001$). There was no significant difference in overall morbidity (17 studies, 14% for resection group versus 15% for non-resection group, HR = 1.14, 95%CI 0.77–1.68, $I^2 = 73\%$) or in the rate of bowel obstruction during treatment (4 studies, 11% for resection group versus 19% for non-

**Table P0923**

| | No Neoplasia | Neoplasia** | Advanced Neoplasia** | | |
|---|---|---|---|---|---|
| | | | | AP (10 mm or more) | CRC |
| Negative test (%)* (n = 444) | 254 (57.2) | 190 (42.8) | 62 (14.0) | 59 (13.3) | 3 (0.7) |
| Positive test (%) (n = 318) | 173 (54.4) | 145 (45.6) | 61 (19.2) | 43 (13.5) | 18 (5.7) |
| Sensitivity (%) (95%CI) | | 43.3 (38.0–48.8) | 49.6 (40.5–58.8) | 42.2 (32.4–52.3) | 85.7(63.7–97.0) |
| Specificity (%) (95%CI) | | 59.5 (54.7–64.2) | 59.8 (55.9–63.6) | 58.3 (54.5–62.1) | 59.5 (55.9–63.1) |
| Positive Predictive Value (%) (95%CI) | | 45.6 (40.0–51.3) | 19.2 (15.0–24.0) | 13.5 (10.0–17.8) | 5.7 (3.4–8.8) |
| Negative Predictive Value (%) (95%CI) | | 57.2 (52.5–61.9) | 86.0 (82.5–89.1) | 86.7 (83.2–89.7) | 99.3 (98.0–99.9) |

CI: Confidence Interval /*Negative test if value for NKA is 200 pg/mL or more / **Neoplasia = all patients with either adenomatous polyps (any size) or CRC; Advanced Neoplasia = all patients with either adenomatous polyps of 10 mm or more or CRC.

resection group, HR = 0.37, 95% CI 0.11–1.23; $I^2$ = 82%). The resection group had a significantly reduced 30-day mortality (18 studies, HR = 0.63, 95% CI 0.42–0.96, $I^2$ = 55%), as well as a reduced risk of death due to any cause (28 studies, HR = 0.51, 95% CI 0.48–0.54, $I^2$ = 80% for adjusted analysis; 12 studies, HR = 0.50, 95% CI 0.44–0.56, $I^2$ = 78% for unadjusted analysis). Heterogeneity was high, although all studies except one estimated improved survival for the resection group.
**Conclusion:** The present level IIb evidence reveals a prognostic benefit for resection of the primary tumor in the palliative treatment of stage IV colorectal cancer patients. However, these results are clearly challenged by a high rate of heterogeneity and only retrospective data reporting. The outcomes of the currently ongoing randomized controlled trials SYNCHRONOUS, GRECCAR 8, and CAIRO 4 are eagerly awaited in order to further elucidate this question.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0925 ARE ENDOSCOPIC SUBMUCOSAL DISSECTIONS OF CECAL TUMOR INVOLVING THE ILEOCECAL VALVE AND APPENDICEAL ORIFICE FEASIBLE?

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**Introduction:** The ileocecal valve (ICV) and the appendiceal orifice (AO) are considered difficult sites for endoscopic tumor resections because of their complicated morphologies[1]. Additionally, little is known about the outcomes of endoscopic submucosal dissection (ESD) of these sites[2].
**Aims & Methods:** The aim of this study was to evaluate the feasibility and outcomes of ESD of ICV and AO lesions as compared to those of the other cecal lesions. This was a multicenter retrospective analysis involving two referral hospitals (Shizuoka Cancer Center, Toshiba Rinkan Hospital). Cecal lesions treated by ESD were divided into three categories: those involving the ICV (ICV), those involving the AO (AO), and those involving other sites (Ce). Rates of procedural success, complications, and recurrences were analyzed. All evaluated cases were followed by at least one surveillance colonoscopy post-operatively. A P value $<.05$ was considered statistically significant; $P>.05$ was considered not significant (n.s.).
**Results:** A total of 115 patients (median age 69 years, 55 women) with cecal lesions (ICV 24, AO 12, and Ce 79) were treated by using ESD between March 2007 and September 2015. Of the 24 ICV lesions, 8 were located on the upper lip, 9 were on the lower lip, and 7 on the both lips. Completion rates of ESD of ICV, AO, and Ce were 100%, 100%, and 95%, respectively (n.s.). En-bloc resection and en-bloc resection + R0 rates were 92% and 83% for ICV, 83% and 75% for AO, and 89% and 73% for Ce, respectively (n.s.). Mean procedural times (min) of ICV, AO, and Ce were 86, 123, and 90, respectively (n.s.). Immediate and delayed perforation rates were 4.2% and 0% for ICV, 8.3% and 0% for AO, and 7.6% and 5.1% for Ce, respectively (n.s.). Two patients with delayed perforation in the Ce group underwent emergent surgery and the others were treated conservatively. Local recurrence occurred in only two patients in the ICV group and in none in the other two groups ($P < .001$). Both patients were treated with surgical resection. Retrospective review of the films revealed poor endoscopic visualization of the proximal tumor margins, and initial surgical margins of ESD specimens were positive in both patients. No stenosis was occurred after ESD in all patients including ICV group.
**Conclusion:** Our results suggest that ESD of lesions involving ICV and AO is a feasible treatment option because the procedural success and complication rates are similar to those of ESD of other cecal lesions. Local recurrence rate after ESD of ICV lesions was significantly higher than that after ESD of other cecal lesions. Therefore, ESD for ICV lesions with poor tumor margin visibility should be done cautiously.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0926 THE PROGNOSTIC FACTORS AND THE IMPACT OF SURGERY ON REDUCING RECURRENCES IN T1 COLORECTAL CANCERS BASED ON A LONG-TERM SURVEILLANCE

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**Introduction:** The recurrence of T1 colorectal cancers is relatively rare, but some cases do develop even after surgery. In addition, their prognostic factors remain obscure.
**Aims & Methods:** The aim of this study is to clarify whether the surgical resection could reduce the risk of recurrence and to investigate the prognostic factors for T1 colorectal cancers by reviewing their long-term outcomes. We analyzed 1050 patients with T1 colorectal cancers resected at our unit from April 2001 to June 2015. Until February 2016, 932 patients were followed up over a mean period of 50.3 months. Of these, 239 cases met the curative criteria for endoscopic resections as follows: well or moderately differentiated adenocarcinoma, no vascular invasion, budding grade 1, slightly invasive submucosal cancer, and negative margin (Group A). The other 693 cases were out of the curative criteria, and initial or additional surgical resection with lymph node dissection was performed in 583 cases (Group B). But 110 cases were followed up without additional surgery because of their complications or refusal (Group C). Disease-free survival was calculated using the Kaplan–Meier method, and the differences were compared using the log-rank test. And also, to clarify the prognostic factors for T1 colorectal carcinomas, we analyzed the association between recurrence and clinicopathological features using the Cox regression analysis.
**Results:** The recurrence rate in Group A was 0% (0/239), 1.03% (6/583) in Group B, and 3.64% (4/110) in Group C. The risk of recurrence in Group C was higher than that in Group B ($p = 0.016$). Among 10 lesions with recurrences, 6 lesions were located in the rectum, and 6 lesions were poorly differentiated adenocarcinoma or mucinous carcinoma ($p = 0.006$, HR = 6.35, and $p = 0.012$, HR = 9.47).
**Conclusion:** Surgical resection reduced the risk of recurrence. But even after surgical resections, some lesions developed recurrences. More careful surveillance is recommended especially for rectal lesions and also lesions with poorly differentiated adenocarcinoma or mucinous carcinoma.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0927 HEPATIC ARTERIAL INFUSION CHEMOTHERAPY FOR UNRESECTABLE LIVER METASTASES OF COLORECTAL CANCER: A MULTICENTER RETROSPECTIVE STUDY

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**Introduction:** Oxaliplatin-based hepatic arterial infusion chemotherapy (HAIC) for the treatment of liver metastases (LM) from colorectal cancer (CRC) is only used in few experienced centers. Our aim was to evaluate the efficacy and the safety of HAIC in a retrospective multicentric study conducted in 4 centers which have developed this technic for 5 years.
**Aims & Methods:** Clinical, biological and radiological data of all patients treated in 4 institutions with HAIC for unresectable LM from CRC from October 2011 to January 2016 were retrospectively analyzed. Toxicity data were graded using the NCI-CTCAE V4.0 classification. RECIST criteria were used for response rate analysis. Progression-free and overall survivals were estimated using the Kaplan-Meier method.
**Results:** Sixty-one patients with unresectable LM from CRC were included. Median age was 58 years (range 30 to 81 years). Patients were treated in first line, second line, third line, fourth line and beyond in respectively 4.9%, 50.8%, 19.7% and 24.6% of cases. Oxaliplatin was used for HAIC and a median of 6 courses (range 1 to 18) has been delivered in combination with systemic 5FU-Leucovorin in 43.3% of patients, or in combination and with 5FU-Leucovorin plus other IV chemotherapies or monoclonal antibodies in 55% of patients. Grade 3–4 clinical toxicities were reported in 16% of patients, including 9.8% of grade 3–4 neurotoxicity. Grade 3–4 biological toxicities were reported in 24.6% of patients including 22.2% of neutropenia. Catheter-related complications were observed in 31.1% of patients. Objective tumor response rate was 21.3%, tumor control rate was 70.5%, and hepatic tumor control rate was 73.7%. Median hepatic progression-free survival (PFS), median PFS and overall survival (OS) were respectively 9.0, 6.0 and 13.8 months. The secondary R0-resection rate was 16.4% with a 2-year survival of 80%.
**Conclusion:** These data confirm the feasibility and the safety of HAIC using oxaliplatin in centers which have recently developed this technic. The results in

term of hepatic PFS, PFS and OS, as well as the rate of secondary resections of LM, are promising.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0928 CHARACTERISTICS OF THE NON-RESPONDER GROUPS OF THE COLORECTAL CANCER SCREENING PILOT STUDY IN LATVIA

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**Introduction:** Colorectal cancer is the third most common cancer worldwide and the most common cancer of the digestive tract both globally and in Latvia. Colorectal cancer screening programme in Latvia is opportunistic and with unacceptably low participation rate. Invitation-based colorectal cancer screening (CRC) pilot study took place in Latvia in 2011.
**Aims & Methods:** The objective of the study was to identify and describe the reasons for unwillingness to participate in colorectal cancer screening in Latvia for the groups of non-participation. The non-responders for a faecal occult blood test-based colorectal cancer screening pilot study in Latvia were addressed by asking them to fill out a questionnaire detecting the reasons for non-participation. 8149 questionnaires were sent to all non-responders. A questionnaire was completed and sent back by post by 1191 respondents (14.7%). The results were weighted by age, gender and place of living. Adjusted odds ratio (OR) and 95% confidence interval (CI) was calculated comparing each group with the rest of the sample.
**Results:** Two main categories of reasons for non-participation were identified: reasons related to patient only and reasons related to screening. Screening-related reasons were divided into two subgroups: test related and screening organization related. Results for patient-related reasons group demonstrated highest proportion of participants in oldest age group 70–74 OR = 1.9 (CI 1.2–3.0), they were living in small town or rural area, OR = 1.5 (CI 1.1–2.1), having no opinion about the screening program OR = 2.2 (CI 1.2–3.8). Patients belonging to this group more likely had not visited their general practice doctor (GP) for a while, OR = 1.7 (CI 1.0–2.8) or even never had visited him or did not have a GP, OR = 28.6 (CI 2.8–295.3). They most likely will not participate in CRC screening next year: answer "very unlikely" OR = 9.1 (CI 4.7–17.5). Test-related group was never informed about screening program, OR = 1.6 (CI 1.0–2.6) and claimed that there is not enough information about screening, OR = 1.7 (CI 1.1–2.7) and more likely received guaiac test OR = 1.7 (CI 1.1–2.6). Screening-related group was informed about screening program by their GPs, OR = 1.4 (CI 1.1–1.6), visited their GPs several times a year, OR = 1.6 (CI 1.1–2.4) and more likely will participate in the CRC next year.
**Conclusion:** Differences in groups' characteristics should be taken into account when organising an information campaign about colorectal cancer screening programme. (The study was funded in part from ESF project 2009/0220/1DP/1.1.1.2.0/09/APIA/VIAA/016).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0929 IMPACT OF EVALUATION OF INDIVIDUALIZED CHEMOTHERAPY FOR COLORECTAL CANCER (CRC) BASED ON COLLAGEN GEL DROPLET-EMBEDDED DRUG SENSITIVITY TEST (CD-DST)

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**Introduction:** The leucovorin (FOL) and fluorouracil (5-FU) plus oxaliplatin (l-OHP; FOLFOX) or FOL and 5-FU plus irinotecan (SN-38; FOLFIRI) are widely used as first-line chemotherapy in the treatment of advanced CRC. However, second-line chemotherapy must be abandoned in certain cases due to disease progression, adverse effects or high medical cost in clinical setting. Therefore, the most effective regimen should be selected as first-line chemotherapy. We reported that individualization of first-line treatment (FOLFOX/FOLFIRI/Dual /Poor responder) was possible using CD-DST and individualized first-line therapy with the CD-DST may improve the prognosis of patients with unresectable CRC, especially in poor responders (UEGW: 2014; P1538, 2015; P1681).
**Aims & Methods:** In this prospective study, we evaluated the overall survival (OS) of super responder and medium responder in dual responder, moreover, adequate first-line chemotherapy group and inadequate first-line chemotherapy group in poor responder. Between Mar. 2008 and Dec. 2015, we obtained tumor specimens from 120 CRC patients without preoperative chemotherapy. 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 $\mu$g/ml, respectively) and 5-FU and SN-38 (6.0 and 0.2 $\mu$g/ml, respectively). The cumulative distribution of IR values under each condition was evaluated on the basis that the clinical response to FOLFOX and FOLFIRI is equivalent (approximately 50%). [1] All patients were divided into 4 cohorts: FOLFOX and FOLFIRI responder (dual responder), FOLFOX responder, FOLFIRI responder, and poor responder. Dual responder were divided into 2 cohorts: super responder (the upper 15.9%: one standard deviation) and medium responder. [2] All patients were divided into 3 cohorts: FOLFOX recommended, FOLFIRI recommended, and both regimens recommended. First-line regimens were selected by the attending physician. The OS of super responder and medium responder in dual responder, moreover, the group treated with adequate first-line chemotherapy and the group treated with inadequate first-line chemotherapy in poor responder were evaluated Kaplan-Meier method.
**Results:** In 2 regimens, the distributions of IR% in all patients showed the normal distribution. There were 39 unresectable CRC patients with chemotherapy. [1] In 4 cohorts: The median survival time (MST) of dual responders (n21) and poor responders (n13) was 1,025 and 810 days, respectively. The MST of super responders (n11) and medium responders (n10) was 927 and 1025 days, respectively. The long-term survivor (over 2700 days) belonged to only super responder. [2] In 3 cohorts: In poor responder, the MST of the group treated with adequate first-line chemotherapy (n5) and the group treated with inadequate first-line chemotherapy (n8) was 810 and 337 days, respectively (p = 0.02), moreover, the frequency of chemotherapy of the group treated with adequate first-line chemotherapy and the group treated with inadequate first-line chemotherapy was 22.8 and 11.0 times days, respectively (p = 0.04). Limitation: The periods of observation of 4 patients in super responder were less than 150 days.
**Conclusion:** Administration of the recommended first-line regimen using CD-DST for unresectable CRC patient is important for improvement in the further prognosis. It is most important to administrate adequate first-line regimen, especially in poor responders.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0930 DOES STENTING AS A 'BRIDGE TO SURGERY' IN LEFT-SIDED COLORECTAL CANCER OBSTRUCTION REALLY WORSEN ONCOLOGICAL OUTCOMES?

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**Introduction:** Self-expandable metal stents (SEMS) for colonic decompression were first introduced for palliative purposes in patients with obstructing rectal cancer [1]. Thereafter, indications of SEMS have been expanded to their use as a 'bridge to surgery', relieving colonic obstruction before surgical resection [2]. However, it is still unclear whether SEMS as a bridge to surgery benefits patients with left-sided CRC obstruction [3–7].
**Aims & Methods:** This study therefore compared outcomes of SEMS as a bridge to surgery (SEMS group) and direct surgery (OP group) in patients with left-sided CRC obstruction. Of 113 patients who underwent curative surgery for left-sided CRC obstruction at Asan Medical Center between 2005 and 2011, 42 underwent direct surgery and 71 underwent SEMS insertion followed by elective surgery. After 1:1 propensity score matching, 42 patients were enrolled in both the SEMS and OP groups, and their postsurgical outcomes were compared.
**Results:** The 3 and 5 year overall survival rates were similar in the SEMS (87.0% and 71.0%, respectively) and OP (76.4% and 76.4%, respectively) groups (P = 0.931; Fig. 2a). Similarly, the 3 and 5 year recurrence-free survival rates were similar in the SEMS (91.9% and 66.4%, respectively) and OP (81.2% and 71.2%, respectively) groups (P = 0.581). Only one of the 42 patients in the SEMS group experienced a technical failure of the SEMS, making the technical success rate 97.6%. The clinical success rate of SEMS was 92.9%. SEMS-associated perforation occurred in two patients (4.8%). Elective surgery was performed a median 13.5 (interquartile range, 11.0) days following SEMS insertion. Analysis of CRC surgery showed that six patients in the OP group and three in the SEMS group required two-stage operations, a difference that was not statistically significant (P = 0.483). The rate of temporary stoma formation at discharge was similar in the two groups. Postsurgical complication rates were similar in the SEMS and OP groups (9.5% vs. 16.7%, P = 0.344). The need for postoperative admission to the intensive care unit and the median length of hospital stay following surgery were similar in the two groups.
**Conclusion:** In conclusion, these findings suggest that, if inserted cautiously by qualified endoscopists, SEMS as a bridge to surgery does not have deleterious effects on long-term oncological outcomes in patients with left-sided CRC obstruction and can achieve similar outcomes to the direct surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Abstract No: P0934**
**Table 1.**

| Median (IQR) | HV | IBS-C | IBS-D | IBS-M | P value |
|---|---|---|---|---|---|
| Fasting small bowel water (mL) | 44 (15–70) | 61 (23–87) | 20 (10–47)[a,b] | 21 (10–35)[a,b] | <0.01 (Kruskal-Wallis) |
| AUC post prandial small bowel water (L*min) | 24.1 (12.8–29.5) | 13.8 (9.4–24.4) | 13.8 (8.6–18.2) [a] | 12.3 (9.1–19.3) [a] | <0.01 (Kruskal-Wallis) |
| Fasting transverse colon volume (mL) | 165 (117–255) | 253 (200–329)[a] | 212 (103–274)[b] | 169 (119–227)[b] | 0.02 (Kruskal-Wallis) |
| Area under the curve for postprandial total colonic volume (t = 0 to t = 360 min) L*min | 179.7 (137.3–231.4) | 224.0 (190.1–251.1)[a] | 172.8 (139.2- 232.1)[b] | 171.2 (145.8- 216.9) | Kruskal-Wallis p = 0.06 |
| WGTT (h) | 34 (4–63) | 69 (51–111)[a] | 34 (10–77)[b] | 34 (19–81) | 0.06 (Kruskal-Wallis) |

[a]$p < 0.05$ versus HV, [b]$p < 0.05$ versus IBS-C


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## P0931 EFFICACY AND SAFETY OF ENDOSCOPIC COLONIC STENTING: A RETROSPECTIVE COMPARISON OF WALLFLEX AND NITI-S COLONIC STENTS


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**Introduction:** Endoscopic stenting with self-expandable metal stents (SEMS) is often performed as a bridge to surgery (BTS) or as palliative therapy (PAL) for malignant colorectal obstruction. This procedure was covered by the National Health Insurance of Japan in January 2012, and now the WallFlex colonic stent and Niti-S colonic stent can be used in Japan. This study aimed to compare the efficacy and safety of the WallFlex colonic stent and the Niti-S colonic stent.
**Aims & Methods:** A total of 78 patients (82 lesions, male/female: 34/38, average age: 73.6 years) underwent endoscopic SEMS placement between November 2011 and April 2016 at Kure Medical Center and Chugoku Cancer Center. The WallFlex colonic stent was used in 36 patients (38 lesions: Group W), and the Niti-S colonic stent, in 42 patients (44 lesions: Group N). Stratified analysis of clinical background, technical success rate, procedure time, clinical success rate, and complications was performed to compare Group W with Group N.
**Results:** Endoscopic SEMS placement was attempted in 78 patients (BTS: 46 patients [59%], PAL: 32 patients [41%]). In Group W, an SEMS was placed in 18 patients (50%) as BTS and in 18 patients (50%) as PAL; in Group N, an SEMS was placed in 28 patients (67%) as BTS and in 14 patients (33%) as PAL. The technical success rate was 100% in both groups. The overall clinical success rate was 91% (71/78): 86% (31/36) in Group W and 95% (40/42) in Group N. Complications within 7 days included abdominal pain (3/36, 8%), poor expansion (1/36, 3%), and fever (1/36, 3%) in Group W, and perforation due to obstructive colitis (2/42, 5%) in Group N. Complications after 8 days included stent-related perforations (4/35, 11%) and stent occlusion (1/35, 3%) in Group W and stent occlusion (2/40, 5%) in Group N. Three patients with stent occlusion were treated with in-stent restenosis using an SEMS, and obstruction-related symptoms improved in all 3 cases. All 4 patients with stent-related perforations had undergone palliative stenting with the WallFlex colonic stent, and the stent-related perforation rate in Group W was significantly higher than that in Group N. On retrospective analysis, predicting perforation on the basis of diagnostic imaging would have been difficult in 2 cases of perforation due to obstructive colitis in Group N. However, 1 of the 2 patients had extreme abdominal pain, with high lactic acid levels on blood gas analysis. The other patient received chemotherapy, including bevacizumab, before obstructive colitis. The median stent patency period was 105.5 days (range 0–942 days) in the palliative stent population; 72% (23/32) of patients maintained stent patency until death or end of follow-up. There was no significant difference in stent patency probability between Group W and Group N.
**Conclusion:** Technical and clinical success rates were very high in both groups. The risk of stent-related perforation was lower when using the Niti-S stent. However, in cases of obstructive colitis, because it is difficult to predict perforation by diagnostic imaging, the risk of perforation should be carefully evaluated with reference to diagnostic indications such as lactic acid levels.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0932 TINED LEAD TEST STIMULATION TO PREDICT LONG-TERM BENEFIT FROM SACRAL NERVE STIMULATION IN PATIENTS WITH CHRONIC CONSTIPATION (TILTS-CC)


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**Introduction:** The primary objective was to assess the value of the tined lead active/sham testing to predict long-term benefits of sacral nerve stimulation (SNS) for patients with chronic constipation. Secondary objectives included quantifying placebo response during temporary testing, efficacy of permanent SNS, any baseline predictors of response and the effect of SNS on quality of life.
**Aims & Methods:** This study used a randomised double-blind 2-period cross-over design. Tined lead testing was performed over a 6-week period. The cross-over design alternated each patient between ACTIVE and SHAM sub-sensory stimulation periods with an intervening washout. Based on response to treatment patients were classified as discriminate responder (improved with ACTIVE only), indiscriminate responder (improved with SHAM) or non-responder. Discriminate or indiscriminate responders proceeded to IPG (implanted pulse generator) and permanent SNS. Follow-up was for 6 months in all patients with a 3-month assessment in IPG patients.
**Results:** 45 patients were randomised, of whom 29 (64.4%) were responders to the testing phase. Of these, 27 were implanted with a permanent IPG. During the testing phase, 7 (18%) were discriminate responders, 22 (56%) were indiscriminate responders and 10 (26%) were non-responders. At 6 months there was no significant difference between discriminate and indiscriminate responders (60% vs 57%, p = 0.76) in the primary endpoint (a => 0.5 reduction in PAC SYM). Results showed no significant differences during the testing phase by timing or sequence, supporting the success of blinding. The study was terminated prematurely due to a persistent and unacceptably high serious infection rate: 10 infections, of which 9 were severe and led to removal of the lead (n = 6) or IPG (n = 3). Among permanently implanted patients there was a modest improvement in PAC SYM (−1.03, 95%CI −1.39 to −0.07) at 3 months, but benefit reduced by 6 months (−0.69, 95%CI −1.00 to −0.37).
**Conclusion:** In patients with constipation: (1) temporary testing is a poor predictor of response to SNS at 6 months; (2) there appears to be a strong and prolonged placebo response to both the testing phase and follow-up; (3) the extended testing period is associated with unacceptably high infection rates. Prolonged failure to recruit to the planned sample size and small sub-group numbers mean that further conclusions about SNS benefit at 6 months cannot be drawn. This abstract presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-1010-23212). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
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C.H. Knowles: Professor Knowles has received fees for regular consultancy as part of the Medtronic Global Expert Panel for GI/GU' + speaker payments
All other authors have declared no conflicts of interest.

## P0933 SYN-010, A PROPRIETARY MODIFIED-RELEASE FORMULATION OF LOVASTATIN LACTONE, LOWERED BREATH METHANE AND IMPROVED STOOL FREQUENCY IN PATIENTS WITH IBS-C: RESULTS OF A MULTI-CENTRE RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED PHASE 2 A TRIAL

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**Introduction:** Observational studies show a strong association between delayed intestinal transit and intestinal methane production. Experimental data suggest a direct inhibitory activity of methane on the colonic and ileal smooth muscle. The archaeon *Methanobrevibacter smithii* is the predominant methanogen in the human intestine. Certain statins can inhibit archaeal methane production without affecting other gut organisms as demonstrated in livestock and humans.

**Aims & Methods:** The aim of this trial (NCT02495623) is to assess the efficacy of a proprietary modified release lovastatin lactone in lowering intestinal methane production. Subjects with irritable bowel syndrome with constipation (IBS-C) and a breath methane value >10 parts per million (ppm) at screening were randomly assigned to receive placebo, SYN-010 dose 21 mg or SYN-010 dose 42 mg orally once daily for 28 days. The primary endpoint was the change from baseline in the area under the curve (AUC) of breath methane production at Day 7, based on a 180-minute lactulose breath test (LBT). Secondary efficacy assessments included change in methane AUC at Day 28, stool frequency and consistency, abdominal pain, bloating, and safety data. A necessary normalisation of the severely left-skewed breath test data, not pre-specified in the statistical analysis plan, was accomplished by square root transformation; paired t-tests were performed allowing each subject to serve as their own control. The analyses of the clinical outcomes were performed with untransformed raw data.

**Results:** 63 subjects were enrolled in the trial. After 7 days statistically significant (SS) reductions in breath methane levels were seen in the 42 mg dose arm ($p = 0.02$ but not the 21 mg dose arm ($p = 0.64$). In contrast, after 28 days both dose arms, 21 mg and 42 mg, showed SS reductions ($\Delta$) of breath methane levels, except for placebo (Table). Placebo $\Delta$ – 31.0, $p = 0.15$, SD 74.3; 21 mg dose $\Delta$ – 22.6, $p = 0.03$, SD 55.0; 42 mg dose $\Delta$ −34.3, $p = 0.01$, SD 59.0; Unit: ppm*hours. Percentage of weekly abdominal pain intensity and stool frequency responses are shown in the Table. The definition of these outcomes are consistent with the FDA IBS guidance. A SS improvement in the stool frequency response for the 21 mg dose group was apparent. The 42 mg dose group was numerically better (see Table). No serious adverse events were observed.

Breath Methane and Clinical Outcomes

| | Dose | Placebo | 21 mg | 42 mg | Combined |
|---|---|---|---|---|---|
| | Number | 22 | 22 | 19 | 41 |
| | Decrease in Methane | | | | |
| **Day 7** | Mean (SD) | -10.6 (53.5) | 11.2 (52.4) | -34.6 (63.7) | |
| | p-value | 0.88 | 0.64 | 0.02 | |
| **Day 28** | Mean (SD) | -31.0 (74.3) | -22.6 (55.0) | -34.3 (59.0) | |
| | p-value | 0.11 | 0.03 | 0.009 | |
| | Abdominal Pain Intensity Response (Improvement)* | | | | |
| | Mean (SD) | 10.7 (30.2) | 14.8 (25.2) | 29.0 (37.9) | 21.3 (32.1) |
| | p-value | - | 0.26 | 0.08 | 0.11 |
| | Stool Frequency Response (Improvement)** | | | | |
| | Mean (SD) | 16.3 (22.8) | 41.3 (36.5) | 22.4 (28.7) | 32.5 (34.1) |
| | p-value | - | 0.02 | 0.54 | 0.07 |

*An Abdominal Pain Intensity Weekly Responder is defined as a patient who experiences a decrease in the weekly average of worst abdominal pain in the past 24 hours score (measured daily) of at least 30 percent compared with baseline weekly average. **A Stool Frequency Weekly Responder is defined as a patient who experiences an increase of at least one complete spontaneous bowel movement (CSBM) per week from baseline.

**Conclusion:** This is one of the first trials to target a specific component of the intestinal microbiome. It shows that SYN-010 has the potential to reduce intestinal methane production as measured by breath test in patients with IBS-C. This study was not powered to show improvement in clinical parameters. The unexpected finding of SS improvement in stool frequency response for the 21 mg dose group and encouraging trends in other clinical parameters are therefore particularly noteworthy. Further development of SYN-010 appears warranted.

**Disclosure of Interest:** K. Gottlieb: Employee and shareholder Synthetic Biologics Inc
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All other authors have declared no conflicts of interest.

## P0934 A DIFFERENT MECHANISMS OF DISEASE IN SUBTYPES IRRITABLE BOWEL SYNDROME AS DEMONSTRATED BY MRI

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**Introduction:** Irritable bowel syndrome (IBS) is a heterogenous condition. Non-invasive biomarkers which could identify the mechanism of disease in subtypes of IBS coud be valuable.

**Aims & Methods:** Our aim was to assess gut transit, small bowel water content and colonic regional volumes of different clinically defined IBS subtypes both fasted and post-prandially using MRI scans. 34 healthy volunteers (HV), 30 IBS with diarrhoea (IBS-D), 16 IBS with constipation (IBS-C) and 11 IBS with mixed bowel habit (IBS-M) underwent whole gut transit and small and large bowel volumes assessment with MRI scans from $t = 0$ to $t = 360$ min.

**Results:** Median (IQR)**:** See table 1. Fasting small bowel water content in IBS-D and IBS-M were 20 (10–47) and 21 (10–35), significantly less than HV at 44 (15–70) mL, $p = 0.02$ as was the postprandial area under the curve (AUC) $p < 0.01$. The fasting transverse colon volumes in IBS-C were significantly larger at 253 (200–329) compared to HV, IBS-D and IBS-M whose values were 165 (117–255), 212 (103–274) and 169 (119–227) mL respectively, $p = 0.02$. Whole gut transit time (WGTT) for IBS-C was prolonged at 69 (51–111), compared to HV at 34 (4–63) and IBS-D at 34 (10–77) h, $p = 0.02$. Bloating score (VAS 0–10 cm) correlated with transverse colon volume at $t = 405$ min, Spearman $r = 0.21$, $p = 0.04$.

**Conclusion:** The constricted small bowel in IBS-D & IBS-M and the dilated transverse colon in IBS-C point to significant differences in underlying mechanisms of disease.

**Disclosure of Interest:** R. Spiller: I have received research funding from Lesaffre and Ironwood and free drug for clinical trial from Norgine. I also acted on Advisory Boards for Almirall, Astellas, Ibsen and Danone.
All other authors have declared no conflicts of interest.

## P0935 ABNORMAL BALLOON EVACUATION TEST DOES NOT IDENTIFY WHICH PATIENTS WILL RESPOND TO BIOFEEDBACK; ANORECTAL MANOMETRY OR EMG, AND STRUCTURAL EVALUATION ARE NEEDED

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**Introduction:** The utility of anorectal manometry (ARM) and pelvic floor EMG for diagnosing functional defecation disorder and selecting patients for biofeedback treatment has been challenged. Our aim was to determine whether patients with different causes of difficult defecation are equally responsive to biofeedback.

**Aims & Methods:** In 132 patients with an abnormal balloon evacuation test (BET > 2 min) and fewer than 3 complete spontaneous bowel movements per week (CSBM), digital rectal examination, ARM, pelvic floor EMG, and defecography were used to classify 33 as obstructed defecation (OD), 20 as dyssynergic defecation only (DD; paradoxical contraction or inability to relax pelvic floor muscles when attempting to defecate), 10 as inadequate rectal propulsion only (IRP; rectal pressure <45 mmHg when attempting to defecate), and 67 as combined DD and IRP (DD/IRP). A nurse who was unaware of the diagnostic test results provided all patients with 5 biofeedback training sessions designed to teach relaxation of pelvic floor muscles simultaneously with contraction of abdominal wall muscles when evacuating. Primary outcomes were self-ratings of improvement in constipation symptoms on a 7-point scale (“markedly worse” to “markedly better”), and changes in CSBMs.

**Results:** (1) OD patients reported less improvement ($p < .001$) than DD, IRP, or DD/IRP patients, which were similar to each other. (2) OD patients increased CSBMs by a smaller amount than the other 3 groups ($p < .001$), which were similar. (3) Most other symptoms of difficult defecation (straining, hard stools, sensations of incomplete defecation or anal obstruction, <3 stools/week, painful defecation, Bristol Stool Scale scores, and ratings of life interference) improved less in the OD group compared to the other groups (all $p < .05$). (4) Anal canal resting and squeeze pressures and rectal sensory thresholds revealed no differences between groups.

**Conclusion:** The BET is insufficient for identifying patients who should be treated with biofeedback. Physical examination, ARM, EMG, and defecography provide additional utility.

**Disclosure of Interest:** G. Chiarioni: Speaker and/or Board Consulter for Shire Italia and Takeda Italia, Member of the Anorectal Committee of the Rome Foundation
All other authors have declared no conflicts of interest.

## P0936 SIGNIFICANCE OF PUSH TEST AND BALLON EXPULSION TEST ESTABLISHED BY HIGH-RESOLUTION ANORECTAL MANOMETRY (HRAM) AND ITS SIGNIFICANCE FOR DYSSYNERGIC DEFECATION DIAGNOSTICS

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**Introduction:** The lack of disclosure of the external anal sphincter (AS), or a paradoxical tension during the push test and inability of the patient to expel the balloon from the rectum considered as direct evidence of dyssynergic defecation by some researchers. Meanwhile other authors detect these patterns in healthy individuals. It is of interest to determine the importance of these parameters for the diagnosis of dyssynergia of the pelvic floor muscles.

**Aims & Methods:** To determine the frequency of dyssynergia and its prevalent type in asymptomatic healthy subjects. 26 asymptomatic healthy adults (18 women, 8 men) median age was 35.03 years (19–59) were studied. We performed them a high-resolution anorectal manometry (HRAM) using a 20 channels silicone water-perfused catheter (Solar GI, MMS, Netherlands). The following HRAM parameters were analyzed: push relaxation percentage of external anal sphincter (EAS) during push test, success of balloon expulsion test (BET) on left lateral decubitus position with latex balloon inflated to 50 mL. The statistical analyses were performed using Statistica for Windows 6.0 (StatSoft Inc.).

**Results:** Push relaxation percentage of EAS was 21.38 (-38.1; 77.3). According to dyssynergia classification (Rao S., 2004) signs of dyssynergia were identified in 9 persons (34.6%): I type was established in 6 (23.08%), type III in 3 persons (11.5%). 15 subjects (57.7%) were not able to expel the balloon. Push relaxation of EAS was positively correlated with successful results of BET ($r = 0.61$, $P = 0.001$) and positively correlated with I type of dyssynergia ($r = 0.77$, $P = 0.00$).

**Conclusion:** In asymptomatic healthy adults investigation by HRAM revealed signs of dyssynergia of pelvic floor muscles (predominantly I type). More than half of the subjects failed to comply with the expulsion of the balloon from the rectum. Therefore, these indicators cannot be considered as the only diagnostic criteria of dyssynergic defecation and should be confirmed by other methods of the pelvic floor muscles functional state examination.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0937 IMPROVEMENT OF BOWEL HABITS AND PATIENT'S SATISFACTION – A POOLED ANALYSIS OF MOST RECENT BISACODYL AND SODIUM PICOSULFATE TRIALS

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**Introduction:** The prescription-free laxatives bisacodyl (BIS) and sodium picosulfate (SPS) are metabolized to form the same locally acting active metabolite bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM). Both laxatives are well recognised as safe and effective treatment options for patients suffering from constipation.

**Aims & Methods:** The aim of this post-hoc analysis was to investigate the extent to which diphenyl methane laxatives (BIS/SPS) lead to objective (bowel movement frequency) and subjective improvements (Patient Assessment of Constipation Quality of Life (PAC-QOL©)) in patients suffering from chronic constipation (Rome III criteria). A pooled analysis was performed with the two recent clinical trials [1, 2], in which a total of 735 patients were randomized in a SPS/BIS:placebo ratio of 2:1. The analysis is based on 718 (SPS/BIS: 468, placebo: 250) patients constituting the full analysis set (FAS) = treated patients providing post-treatment data for the primary endpoint 'mean number of complete spontaneous bowel movements (CSBMs)/week over 4 weeks'.

**Results:** With laxative treatment, the mean number of CSBMs/week increased from 1.0 (baseline week) to a weekly mean of 4.4 over 4 weeks compared to an increase from 1.1 to 1.8 with placebo. Over the 4 weeks of treatment, 59.4% of laxative treated patients achieved a mean number of $\geq 3$ CSBMs/week compared to only 22.4% in the placebo group.

The PAC-QOL© overall score as well as all four subscale scores improved remarkably stronger after 4 weeks of treatment with BIS/SPS compared to placebo ($p < 0.0001$ for all). The items showing the highest odds ratio (OR) within each of the main four subscales were: "physical discomfort": feeling of heaviness (OR = 5.9), "psychosocial discomfort": eating less and less (OR = 3.0), "worries and concerns": being more and more bothered by not being able to open bowels (OR = 3.8) and "satisfaction": having had fewer bowel movements than desired (OR = 7.6).

The highest mean treatment difference between BIS/SPS and placebo was observed in the subscale "satisfaction" with the corresponding single PAC-QOL© items providing odds ratios in the range of 4.2 to 7.6. Notably, 64.3% of the patients in the active group showed a clinically relevant improvement $\geq 1$ point [3] in PAC-QOL© subscore "satisfaction" compared with 26.1% receiving placebo ($p < 0.0001$). Those results are in the range of improvements to be seen with prescription laxatives such as prucalopride for which corresponding improvements in this PAC-QOL© subscore were reported in 45.8% of the treated patients compared with 21.5% with placebo [4].

**Conclusion:** The data analysed show that chronic constipated patients receiving bisacodyl or sodium picosulfate experienced a significant improvement in their bowel habits and in their disease-related quality of life compared to placebo. Thus, the diphenyl methane laxatives investigated were demonstrated to offer a significant benefit for constipated patients not only with respect to the laxative effect itself but also in terms of their well-being.

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H. Weigmann: Employee of Boehringer Ingelheim
E. Richter: Employee of Boehringer Ingelheim
P. Kammann: Employee of Boehringer Ingelheim

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## P0938 GOOD AGREEMENT BETWEEN ORO-ANAL TRANSIT TIME MEASURED BY WIRELESS MOTILITY CAPSULE AND RADIOPAQUE MARKERS IN PATIENTS WITH FUNCTIONAL BOWEL DISORDERS

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**Introduction:** The wireless motility capsule (WMC) is a relatively new technique for transit measurements, where most studies performed until now have compared the agreement with scintigraphy or radiopaque markers (ROM) studies in cohorts of constipated patients, but less so in patients with other bowel habits.

**Aims & Methods:** The aim of this study was to evaluate the agreement between oroanal transit time (OATT) measured with WMC and ROM, and to describe segmental transit time in patients with functional bowel disorders (FBD) with different predominant bowel habits. We prospectively included patients with a FBD (Rome III criteria). Both procedures were performed during the same time period with the WMC study starting day 1 and the ROM study starting day 2. Medications with an effect on GI motility were discontinued at least 48 h before the investigations. On day 1, the patients swallowed a WMC after ingesting a standardized energy bar (260 kcal). Six hours later the patients were allowed to continue with their habitual diet. Day 2–6 the patients swallowed 10 ROM in the morning, day 7 the intake of ROM was divided into 5 in the morning and 5 in the evening in order to optimize detection of accelerated transit. Flouroscopy was used in the morning of day 8 to count the remaining ROM. OATT was categorized as normal, accelerated or delayed by use of normal values for healthy men and women without GI symptoms(1, 2).

**Results:** We included 52 patients with a FBD (41 women), median age 39 (range 20–69) years): 43 (83%) patients had irritable bowel syndrome (IBS) (constipation (IBS-C) 22, diarrhea (IBS-C) 13, mixed bowel habits (IBS-M) 8) and 9 (17%) had functional constipation (FC). One patient could not swallow the WMC and three patients did not complete the WMC study because of a long transit time (categorized as delayed transit). Two patients chose not to start the ROM investigation, which means that we had complete data from 48 WMC studies and 50 ROM studies. Segmental transit times measured by the WMC are shown in Table 1. FC patients had longer gastric emptying time than IBS-D ($p = 0.003$) and IBS-M ($p = 0.02$). There were no differences in small bowel transit time between the groups. FC patients also had longer colonic transit time (CTT) and OATT than all the IBS subgroups, IBS-C ($p = 0.02$ and 0.01 respectively), IBS-D ($p = 0.001$ for both) and IBS-M ($p = 0.002$ for both). Additionally, IBS-C patients had longer CTT and OATT than IBS-D ($p = 0.01$ for both). Among the 47 patients who had evaluable data from both investigations there was a significant correlation between OATT measured by the WMC and ROM (Spearmańs rho 0.56; $p < 0.0001$), and the classification of OATT (accelerated-normal-slow) was identical in 42 of 49 patients (Cohens kappa = 0.70; $p < 0.0001$) that could be classified by both investigation types.

**Table 1:** Segmental transit (median (range)) measured with WMC (GET = Gastric emptying time, SBTT = Small bowel transit time, CTT = Colonic transit time, OATT = Oro-anal transit time).

| | GET (h) | SBTT (h) | CTT (h) | OATT (h) |
|---|---|---|---|---|
| IBS-C | 2.6 (0.7–19.7)$_{n=22}$ | 4.7 (3–11) $_{n=22}$ | 31 (0.6–156)$_{n=20}$ | 49 (12–167)$_{n=20}$ |
| IBS-D | 2.3 (1.1–4.5)$_{n=13}$ | 4.2 (1.4–6.3)$_{n=13}$ | 19 (4–68) $_{n=13}$ | 25 (10–72)$_{n=13}$ |
| IBS-M | 2.3 (1.3–4) $_{n=7}$ | 5.6 (3.6–7.4)$_{n=7}$ | 22 (16–42) $_{n=7}$ | 29 (24–51) $_{n=7}$ |
| FC | 3.6 (2.7–7.2)$_{n=9}$ | 5.6 (3.5–22)$_{n=9}$ | 87 (44–216)$_{n=7}$ | 108 (53–223)$_{n=7}$ |

**Conclusion:** There is a good agreement between OATT measured by WMC and ROM in patients with functional bowel disorders, and the vast majority of patients are classified into the same categories of normal or abnormal transit with both techniques. The WMC study was well tolerated by patients with functional bowel disorders and has the advantage of providing additional data regarding segmental transit time, as well as pH and pressure data.

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H. Törnblom: Consultant/Advisory Board member for Almirall, Allergan, Danone and Shire.
All other authors have declared no conflicts of interest.

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### P0939 WHAT IS MISSED AND WHAT IS STILL NEEDED FOR EFFICIENT TREATMENT OF CHRONIC CONSTIPATION?


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**Introduction:** Constipation is a common complaint affecting 15% of the general western population. Abundant treatment options are available, though there is no one suitable treatment option for all. Several national societies have released recommendation for the evaluation and treatment of chronic constipation. However, the common practices of GI specialists (GS) and family practitioners (GP) for treating chronic constipation are not well defined, and there are still unmet needs for effective treatment of constipation.
**Aims & Methods:** Aim: To compare the common practices of GPs and of GS specialist for the treatment of constipation, and to examine the conceived limitations of the available treatment options.
Methods: During January to February 2016, an internet survey was sent nationwide and at random to 290 GS and 1312 GPs to assess how treatment strategies and limitations for treatment options for constipation. We assessed for the burden of constipation, indications for referral for a GI consultation, criteria for treatment selection and main unmet needs.
**Results:** 40 GI specialists (18%) and 132 FP (10%) returned the questionnaire. Both groups treat 10–11 patients/week (mean age 41–50 years). The common indications for GI consultation were presence of warning signs (weight loss in26%, new onset constipation 17%, occult blood loss 16%, rectal bleeding 16%, anemia 12%) and unresponsiveness to therapy (24%). Both GPs and GS stated that the most desired effect of therapy was improvement in number of bowel movements and bloating, followed by rapid improvement in the GPs and desire for prescription of the same medication by the GS. GS regularly used polyethylene glycol as first line of therapy, biascodyl as second line and Prucalopride as a third line. GPs used osmotic laxatives (PEG and lactulose) and biascodyl as treatment options for all 3 lines off therapy. About 56% of the GS and 50% of the GPs stated that they would consider prescribing a new medication, if it had high efficacy, rapid action and did not cause addictive response.
**Conclusion:** The awareness to the possible treatment options and to the recommended order of prescription differs between GS and GPs. There are still unmet needs for optimizing the treatment of constipation.
**Disclosure of Interest:** D. Carter: Takeda: Advisory board and speaker fee
R. Dickman: Takeda: Advisory board

### P0940 EXTERNAL AND INTERNAL GUT IMAGING FOR MORPHO-FUNCTIONAL EVALUATION OF THE GUT


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**Introduction:** Automatic and non-invasive diagnostic methods for the evaluation of digestive function have been developed in our laboratory using images obtained by internal (endoscopic capsule) and external (abdominal magnetic resonance) imaging techniques. We applied these combined methodologies to patients with cystic fibrosis. Cystic fibrosis is a multisystem disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The loss of CFTR in the gut results in a dehydrated and acidified intestinal milieu, which consequently impairs small bowel motility and clinically manifests as intestinal obstruction and small intestinal bacterial overgrowth. However, intestinal motor dysfunction in CF has only been evidenced by indirect transit tests.
**Aims & Methods:** Aim: To prove the consistency between parameters of gut function detected by external and internal imaging. Methods: Eight patients (3 men, 5 women; age range 23–38 years) with CF were studied on two separate days with the endoscopic motility capsule procedure (PillCam SB2, Given Imaging) and with an abdominal magnetic resonance (MR). Both studies were performed after a 48 h low-residue diet and without bowel preparation. Morpho-functional analysis of the images was performed with specific, previously validated, computer vision programs based on machine learning techniques.
**Results:** Abnormal intestinal motility was detected in six patients (75%) by endoluminal image analysis. Patients with CF exhibited a low number of intestinal contractions as compared to normal values in healthy subjects ($2.0 \pm 0.3$ vs $5.2 \pm 0.3$ contractions/min; $p < 0.001$), less endoluminal motion ($13 \pm 3$ vs $4 \pm 1\%$ static sequences; $p < 0.001$) and greater retention of turbid content ($61 \pm 8$ vs $28 \pm 4\%$ of small bowel images; $p < 0.001$). Ileal perimeter, measured in MR images, correlated inversely with the contractile activity ($R = -0.85$; $p = 0.015$) and with the presence of intraluminal content ($R = 0.80$; $p = 0.030$) measured by endoluminal imaging analysis.
**Conclusion:** Morpho-functional analysis of internal and external imaging techniques reflect analogous views on gut function.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0941 LEVATOR ANI TENDERNESS IN PATIENTS WITH DYSSYNERGIC DEFECATION


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**Introduction:** Recently we reported the surprising finding that patients with levator ani syndrome share many pathophysiologic features with dyssynergic defecation (DD): Among 94 patients with a primary complaint of chronic proctalgia who had tenderness on digital rectal exam, 86%% exhibited paradoxical contraction of pelvic floor muscle when straining to defecate and 87% could not evacuate a 50-ml water-filled balloon. Moreover, improvement in these parameters was associated with reductions in rectal pain
**Aims & Methods:** Aim: To further explore the hypothesis of shared pathophysiology by determining whether patients with DD report tenderness when traction is applied to the levator ani muscles. Methods: 242 patients with chronic constipation referred to an ambulatory GI practice in Verona, Italy, were evaluated by physical examination including palpation of the levator muscles by standard protocol, questionnaire, balloon evacuation test (BET), and (if they failed to respond to fiber treatment) by anorectal manometry (ARM). Patients were diagnosed DD if they failed to relax anal canal pressures and anal EMG on ARM and also failed to evacuate a 50-ml water filled balloon within 2 minutes. The last 148 of 242 referrals had a second physical exam by an independent physician to assess reliability of tenderness assessment.
**Results:** Three subjects were excluded for technical reasons and 41 due to a positive response to fiber supplements, leaving 198 for analysis. Average age was 45 years and 94% were female. Constipation type was DD in 44.4%, normal transit (NT) in 28%, slow transit (ST) in 11%, and outlet obstruction in 14.1%; 5 had dyssynergia on manometry but normal BET. Tenderness on digital rectal exam was reported by 87/198 patients (43.9%). 71.2% of DD reported tenderness compared to 23.4% of patients with other types of constipation ($p < .001$). 73.6% of patients reporting tenderness also reported that they had pain with 25% or more of their defecations vs. 15.3% for those without tenderness ($p < .001$). Patients reporting tenderness were also younger (41.8 vs. 47.6 years, $p = .007$). Two independent physician examiners agreed on the assessment of tenderness in 93.5% of cases.
**Conclusion:** These data provide further support that the pathophysiology of DD is similar to that of levator ani syndrome because 71.2% of patients with DD report tenderness on palpation of the levator ani muscles and 73.6% of those with tenderness during digital rectal exam report pain during defecation. Assessment of levator ani tenderness is reliable (93.5% agreement). [Supported in part by R01 DK31369]
**Disclosure of Interest:** G. Chiarioni: Speaker and/or Board Consulter for Shire Italia and Takeda Italia, Member of the Anorectal Committee of the Rome Foundation
All other authors have declared no conflicts of interest.

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## P0942 POPULATION PREVALENCE OF ROME IV FECAL INCONTINENCE AND ASSOCIATED RISK FACTORS IN THE UNITED STATES (US), CANADA AND THE UNITED KINGDOM (UK)

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**Introduction:** The new Rome IV diagnostic criteria for fecal incontinence (FI) require higher minimum frequency of accidental leakage of stool than the Rome III criteria (2+ times vs. 1+ times a month). The population prevalence of Rome IV FI and associated symptom and demographic risk factors are unknown.

**Aims & Methods:** A three-country general population survey conducted on behalf of the Rome Foundation was used to assess national FI rates, prevalence difference between demographic groups, and the association of FI with stool consistency abnormalities and urge. This secure internet survey included the Rome IV Diagnostic Questionnaire for Adults and demographic questions, and was completed by a sample of individuals age 18 years and older in the US, UK and Canada (2,100 in each country) provided by Qualtrics (Provo, Utah). Quota-based sampling was used to ensure equal proportion of sex (50%/50%) and age groups (40% age 18–39, 40% 40–64, 20% 65+) across countries, and to control education distributions (30% maximum with college degree or equivalent). Chi-Square analysis was used to compare FI rate differences between countries, and demographic and symptom subgroups. Latest national census figures were used to calculate correction weights for age (in 5-year bins) and gender proportions, and to obtain census-adjusted FI prevalence estimates for each country.

**Results:** Data from 5,931 of 6,300 total survey completers were retained for analysis (49.2% female; mean age = 47.4, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after 369 inconsistent responders were eliminated. Sex or age group proportions were not significantly different between countries due to quota-based sampling. Of the total sample, 16.1% reported some FI symptoms, but 3.3% met Rome IV FI criteria. FI rate was higher ($p < 0.05$) in females than males in the UK (3.5% vs. 2.0%) and Canada (4.0% vs. 2.2%), but not in the US (4.0% vs. 4.4%). National raw and census-weighted (in parentheses) FI rates were 4.2% (4.2%) in the US, 3.2% (2.8%) in Canada and 2.7% (3.1%) in the UK. Individuals aged 18–34 and 35–49 years had significantly lower ($p < 0.01$) FI rates compared to those aged 50–64 and 65+ in Canada and the UK (see Table), but those age group differences were not significant in the U.S. Among individuals meeting Rome IV FI criteria, FI prevalence was significantly increased by the presence of frequent (>20% of BMs) loose stools (OR = 9.10, 95% CI = 6.53–12.66), urgency (OR = 10.66, 95% CI = 7.55–15.08), and hard stools (OR = 2.66, 95% CI = 2.00–3.55).

**Table:** General Population Rome IV FI Prevalence Rates in the US, Canada and UK.

| | Age 18–34 | Age 35–49 | Age 50–64 | Age 65+ | Total Sample | Total Sample Census-adjusted |
|---|---|---|---|---|---|---|
| US (n = 1,949) | 3.8% | 3.5% | 4.8% | 4.4% | 4.2%[2] | 4.4% |
| Canada (n = 1,998) | 0.5%[1] | 1.8%[1] | 4.6% | 5.9% | 3.2% | 2.9% |
| UK (n = 1,994) | 1.4%[1] | 1.4%[1] | 4.1% | 4.1% | 2.9% | 3.2% |

[1]Significantly lower than the rate in the 2 older age groups. [2]Significantly higher than the UK rate.

**Conclusion:** This first population assessment of Rome IV fecal incontinence shows that the condition is present in 3–4% of the general adult population. It tends to be more common in women than men and to be more prevalent after age 50. Frequent hard and loose stools and frequent urgency to defecate are all associated with increased FI risk. [Supported by the Rome Foundation]

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All other authors have declared no conflicts of interest.

## P0943 ANAL DYSPLASIA IN HIV INFECTED PATIENTS: LONG-TERM RESULTS FROM A CYTOLOGICAL SCREENING PROGRAM

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**Introduction:** HIV and human papilloma virus (HPV) infection are known risk factors for the development of anal dysplasia (AD). The risk of anal cancer in men who have sex with men (MSM) infected with HIV has increased in the recent years. Current recommendations for AD screening are based on expert opinion and have not proven their benefit yet.

**Aims & Methods:** The authors intend to evaluate the results obtained after implementation of a systematic cytological screening program in a cohort of patients with HIV infection. This is a prospective study of patients receiving anal dysplasia screening in 2011, in a tertiary referral center. Included male patients with HIV infection, age >18 years, MSM or with oral/genital warts. The patients were followed prospectively until March 2016. Descriptive statistics was performed using IBM SPSS Statistics 22.

**Results:** During the period of the study there were 59 patients (mean age 50 ± 5 years, with median of 30 (IQR: 6–65) months duration of HIV infection (51% patients on antiretroviral therapy)). The median follow-up time was 49 (IQR: 47–53) months (lost follow-up in 9 cases). The results of the initial anal cytology tests were: 40 (71%) negative for intraepithelial lesion or malignancy (NILM), 6 (11%) atypical squamous cells of uncertain significance (ASCUS), 8 (14%) low-grade squamous intraepithelial lesion (LSIL) and 2 (4%) high-grade squamous intraepithelial lesion (HSIL). During follow-up, 27 (46%) patients were referred to proctology consultation and in 19 (32%) cases excision/biopsy of a suspicious lesions on anoscopy was performed. During follow-up, were detected 13 (22%) cases of AD: 7 (54%) low-grade dysplasia (LGD), 4 (31%) high-grade dysplasia (HGD) and 2 (15%) carcinoma in situ (CIS). All patients with HGD were treated with argon plasma destruction and the patients with CIS were treated with combination of radiotherapy and chemotherapy.

**Conclusion:** The implementation of an AD screening programme in HIV infected male patients, MSM or with oral/genital warts, may prevent morbidity and mortality associated with delayed diagnosis of anal cancer. More studies are necessary in order to determine the periodicity of screening programs and evaluate its cost-effectiveness.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0944 ANAL CONDYLOMAS: PREDICTORS OF RECURRENCE AND PROGRESSION TO HIGH-GRADE DYSPLASIA / CARCINOMA IN SITU

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**Introduction:** Anal condylomas with dysplasia are precursors of anal squamous cell carcinoma, appearing in the context of chronic infection with human papilloma virus (HPV). However, there are few studies concerning predictors of recurrence and progression to high-grade lesions (high-grade dysplasia – HGD and carcinoma in situ – CIS).

**Aims & Methods:** The aim was the evaluation of clinical characteristics and predictors of recurrence and progression to HGD / CIS in patients with anal condylomas. We performed a retrospective analysis of all biopsies and subsequent excision of anal condylomas performed in proctology consultation between 2011–2015, in a single center.

**Results:** During the study period 152 biopsies/excisions of anal condylomas were performed in 82 patients followed for 9 ± 12 months. Patients were mostly men (80%) with a mean age of 39 ± 11 years, and 76% had HIV infection (mostly in asymptomatic phase −95%, and under therapy −82%). In 61% of cases there was previous history of condylomas, 39% with prior dysplasia (HGD 65%). The most frequent HPV genotypes were 16 (49%), and 18 (27%). In 66% of biopsies/excisions dysplasia was detected, with 33% of high-grade dysplasia (HGD) and carcinoma in situ in 2%. The most applied treatments included argon plasma (83%) and excision with a scalpel (12%) without evidence of complications. There was a 64% recurrence rate. Presence of HGD/CIS was the sole predictor of recurrence. The predictors of high-grade lesions were shorter time to recurrence ($p = 0.003$), HPV-16 ($p < 0.001$) and previous HGD/CIS ($p = 0.035$).

**Conclusion:** In patients with anal condylomas there is a high frequency of high-grade lesions, including HGD. Such cases need close monitorization due to the

high risk of early recurrence. The identified predictors can aid in the stratification of that surveillance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0945 PHASIC AND CONTINUOUS PROTOCOLS IN ANORECTAL MANOMETRICAL ASSESSMENT OF RECTAL SENSITIVITY: AGREEMENT AND CORRELATION WITH CLINICAL PRESENTATION

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**Introduction:** Anorectal manometry is used in the evaluation of patients presenting with faecal incontinence, constipation or combination of both. It is useful in refining the diagnosis and guiding the management of these disorders. However, there is lack of consensus on the method and interpretation of anorectal manometry. With regards to the assessment of rectal sensitivity by manometry, phasic inflation of the balloon is considered the gold standard, although continuous inflation is now suggested because of the presumably more physiological nature. Cut-off values have only vaguely been defined for both methods of inflation.
**Aims & Methods:** The aim of the present study was to assess correlation and agreement between phasic and continuous methods of manometrical rectal sensitivity assessment, and their correlation with the clinical presentation. We retrospectively assessed rectal sensitivity on anorectal manometry with both phasic and continuous inflation of the anorectal probe in patients presenting to our tertiary care 'Pelvic clinic' with complaints of constipation, faecal incontinence or both. Impaired rectal sensitivity was defined as a first urge to defecation above cut-off value 40 mmHg for phasic and 150 mmHg for continuous inflation. Patients also filled in a questionnaire to correlate their clinical image with results from the two methods of rectal sensitivity assessment.
**Results:** Two hundred and eighty-two patients were included. The inflation pressures associated with first urge to defecation of phasic and continuous methods were significantly correlated (Spearman's rho 0.465, $p < 0.001$). Using the cut-off values stated above, continuous inflation reached sensitivity 16.1% and specificity 97.4% compared to phasic inflation as gold standard. Furthermore, only slight agreement was reached between phasic and continuous inflation using these cut-off values, indicated by Cohen's kappa 0.173. By means of a ROC curve, a new cut-off value of 84.5 mmHg for continuous inflation was defined, yielding the highest Youden index. However, despite this new cut-off value only moderate agreement was reached, indicated by Cohen's kappa 0.429. Impaired rectal sensitivity on phasic inflation was significantly correlated with self-reported constipation ($r_s = 0.151$, $p = 0.001$), manual evacuation of faeces ($r_s = 0.108$, $p = 0.017$) and bloating ($r_s = 0.107$, $p = 0.02$). Impaired rectal sensitivity on continuous inflation was significantly correlated with constipation ($r_s = 0.171$, $p = 0.002$).
**Conclusion:** Our results show a strong correlation between values of continuous and phasic inflation during manometrical rectal sensitivity assessment. However, there is low agreement between the two methods when using currently published cut-off values. Optimizing the cut-off value of continuous inflation increased agreement only moderately. Phasic inflation seems to be correlated with more clinical characteristics of constipation, compared to continuous inflation and thus might be more interesting to use as a diagnostic tool.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0946 THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY AND RECTOANAL DELTA CONTRACTILE INTEGRAL FOR THE ASSESSMENT OF FUNCTIONAL DEFECATORY DISORDERS: TOY OR TOOL?

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**Introduction:** Conventional water perfused manometry (WPM) identifies the functional defecatory disorders (FDD) according to the defecatory patterns suggested by Rao. Unfortunately manometric data are often conflicting with clinical data, and balloon expulsion test (BET) or defecography need to be performed to reach a correct diagnosis. High resolution anorectal manometry (HRAM) and three-dimensional HRAM (3D-HRAM) allow a better evaluation of the endoanal and endorectal pressure and the anorectal dynamics providing a better diagnostic accuracy. On the basis of the indexes used by esophageal high-resolution manometry we identified a new parameter potentially useful for the evaluation of FDD: the Recto-Anal Delta-Contractile Integral (RAD-CI).
**Aims & Methods:** The aims of the study were: – to evaluate the possible correlation between WPM and 3D-HRAM parameters – to evaluate correlation between RAD-CI, traditional Rectoanal gradient (RAG) and BET 21 FDD diagnosed by using WPM, BET and/or defecography (15 type I, 6 type II), underwent 3D-HRAM (Manoscan 360TM, Medtronic – USA). Endoanal and endorectal pressure values obtained during the push straining were used to calculate the contractile integral (CI) which is a measure of duration and intensity. Endoanal CI was evaluated on a space including the anal canal for the whole duration of the push straining. By using the function "isobaric contour" pressures lower than mean resting pressure of the anal canal were excluded. Endorectal CI was calculated on a 10 mm space for the whole duration of push straining. RAD-CI was the difference between endoanal CI (proportionally correlated to 10 mm) and endorectal CI.
**Results:** Correlation between 3D-HRAM and WPM were found regarding: maximum resting ($r = 0.53$, $p < 0.05$), squeeze pressure ($r = 0.85$, $p < 0.001$), RAIR ($r = 0.76$, $p < 0.001$), volume for costant sensation ($r = 0.55$, $p < 0.05$) and maximum tolerated volume ($r = 0.63$, $p = 0.005$). RAD-CI showed significantly lower values in patients with positive BET ($p < 0.05$) (Tab.1).

**Table 1.**

| Correlation with BET | POSITIVE | NEGATIVE | p |
|---|---|---|---|
| RAG (mmHg) | $-50.3 \pm 28.1$ | $-30.1 \pm 28.5$ | 0.17 |
| RAD-CI mmHg*cm*s | $-1259 \pm 221$ | $639.5 \pm 689.2$ | 0.02* |

**Conclusion:** Also in the evaluation in dyssynergia 3D-HRAM shows a substantial agreement with WPM. RAD-CI could be an important index in the evaluation and classification of dyssynergic defecation. This study shows that RAD-CI has a positive correlation with BET, better than RAG. Additional studies are required on a larger number of patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0947 PERCEPTIONS OF CURRENT TREATMENTS FOR FECAL INCONTINENCE

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**Introduction:** Faecal incontinence (FI) is a common and socially stigmatizing condition, but fewer than 30% of people with FI consult for medical or surgical treatment. Multiple behavioral, medical and surgical treatments have been shown to be effective by controlled trials, but data on patients' opinions of these options is limited.
**Aims & Methods:** This study aimed to explore perceptions of the effectiveness and safety of, and willingness to undergo treatment with, sacral nerve stimulation (SNS), biofeedback (BIO), and anal dextranomer injection (INJ) in a population sample reporting FI at least twice per month. Of 254 survey responders, 76 inconsistent responders and 14 subjects previously undergoing BIO, SNS, or INJ were eliminated, leaving 164 for analysis (72%). A 54-question survey enquiring about demographics, FI features and perceptions of BIO, SNS and INJ was distributed online (Qualtrics, Provo, Utah, USA) to individuals with FI in the US general population in March 2016. Perceived effectiveness and safety were rated on a 0–10 scale from "not at all" to "completely" effective or safe, and willingness to undergo each treatment was rated on a 0–10 scale from "definitely not" to "yes, definitely". Free text fields were included to collect data on "worries or concerns" that would prevent the subject from participating in each treatment. FI severity was assessed with the Fecal Incontinence and Constipation Scale (FICA), which has a range of 0–13.
**Results:** Complete data was available for 164 subjects with self-reported FI at least twice per month (112 F, median age 43, range: 18–82). The median FICA score was 8 with 119 (73%) respondents reporting either moderate or severe symptoms (FICA severity score >10). There was no difference in perceived effectiveness scores for SNS, BIO and INJ (means: SNS 5.6, BIO 6.1, INJ 5.7, p = ns). However, BIO was perceived to be safer than INJ ($p < .001$), and INJ was perceived to be safer than SNS ($p < .005$); average safety ratings were SNS 5.0, BIO 7.5, INJ 5.7, $p < .001$). Patients were more willing to try BIO than INJ ($p < .001$) and they were more willing to try INJ than SNS ($p < .005$). Average ratings of willingness to try these treatments if they were offered for free were SNS 5.5, BIO 7.4, INJ 6.2, $p < .001$). Regression analysis demonstrated that greater symptom severity and greater perceived effectiveness significantly predicted willingness to try each treatment ($F[12,151] = 15.23$, $p < .0001$). Free text descriptions of concerns about SNS included infection risk, use of electricity, and potential nerve damage; for BIO, embarrassment, time constraints, and discomfort; and for INJ, risk of infection, damage to the anus, and pain.

**Conclusion:** SNS, BIO and INJ are perceived to be equally effective by individuals with FI in the community. However, due to safety concerns individuals report being more willing to try BIO than either INJ or SNS. Commonly cited fears about accepting treatments for FI include infection, discomfort, and embarrassment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0948 ANORECTAL COMPLICATIONS IN PATIENTS WITH HEMATOLOGIC DISEASES – A SINGLE CENTER EXPERIENCE

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**Introduction:** Proctologic diseases, such as anal sepsis, were responsible for elevated mortality rate (69%) in patients with hematologic diseases.
**Aims & Methods:** Characterization of proctologic diseases in patients with hematologic diseases admitted in the haematology department; analysis of risk factors, therapeutic management and clinical outcome. Retrospective review of all patients admitted to the Haematology Department and observed by anorectal symptoms in the Proctology Departement (January 2010 to September 2015). Analyzed demographic data and clinical outcome, during a 30 days period of follow-up.
**Results:** Eighty-four patients were included, 63.1% (n = 53) males, median age of 56 years. Fifty-four patients (64.3%) were admitted due to acute myeloid leukemia and 82.1% (n = 69) had active hematologic disease. Eighty (95.2%) underwent chemotherapy in previous 15 days. The main proctologic complaints were proctalgia (83.3%, n = 70) and rectal bleeding (46.4%, n = 39). More than half of patients (64.3%, n = 54) had fever and, 67.9% (n = 57), severe neutropenia (< 500 cells/uL). Most patients (67.9%, n = 57) had "no septic" complications: anal fissure, hemorrhoidal disease (including hemorrhoidal thrombosis) and anorectal ulcer, and conservative treatment was adopted, with complete symptoms remission. Twenty-seven patients (32.1%) had "septic" complications: anorectal abscess, perianal fistula and perianal cellulitis; 15 underwent fistula cannulation and seton placement, or surgical drainage/debridement. There were 2 deaths (2.4%), one related to perianal sepsis.
**Conclusion:** In this study, majority of patients had "non-septic" proctologic complications, and had complete symptoms remission with conservative treatment. Surgical debridement or proctologic procedures should be reserved for "septic" complications, which have a better prognosis now than in the past.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0949 POTENTIATION OF LOPERAMIDE AND RACECADOTRIL ANTI-DIARRHOEAL PROPERTIES BY SACCHAROMYCES BOULARDII CNCM I-745 IN A MOUSE MODEL

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**Introduction:** Loperamide and racecadotril are potent anti-diarrhoeal drugs whose mechanisms of action involve the peripheral opioid system in the gut wall. Unlike loperamide that mainly acts on the mu opioid receptor subtypes, racecadotril inhibits enkephalinase and interacts with the delta opioid receptor subtypes (Faure 2013). Main side effects involve constipation for loperamide and headache for racecadotril.
**Aims & Methods:** Our objective was to study the combinations of loperamide or racecadotril with another anti-diarrhoeal drug in order to enhance their anti-diarrhoeal efficacies while reducing concomitantly side effects. For this purpose, the probiotic yeast *Saccharomyces boulardii* CNCM I-745 was combined with loperamide or racecadotril in the model of endotoxins-induced diarrhoea in mice. Diarrhoea was induced by intravenous injection of endotoxins (Lipopolysaccharides from *Escherichia coli*) at 0.25 mg/kg in fasted CD1 mice (Masso et al., 1994). Loperamide (oral route) or racecadotril (intraperitoneal route) and *S. boulardii* (oral route) were given 30 min before endotoxins, and diarrhoea was assessed every hour during 7 hours, according the following score: 0 for clean anus without faeces or with normal faeces, or 1 for soiled anus with unformed or liquid faeces. ED50 of each compound was determined in groups of 12 animals according to the method of Tallarida (2001).
**Results:** Single loperamide administration induced an anti-diarrhoeal effect with ED50s values of $2.62 \pm 0.56$, $3.29 \pm 0.80$ and $4.88 \pm 0.73$ mg/kg at 1, 2 and 7 h respectively after injection of endotoxins. Single S. boulardii administration decreased the percentage of mice showing diarrhoea by around 50% at the doses of 2 and 3 g/kg, one hour after endotoxins injection. Combination of several doses of loperamide with S. boulardii at 3 g/kg showed a significant reduction of loperamide ED50s with anti-diarrhoeal values of $0.76 \pm 0.16$, $0.82 \pm 0.18$ and $0.97 \pm 0.17$ mg/kg at 1, 2 and 7 h respectively, after endotoxins injection. This combination allowed to reduce at least 3 fold the loperamide administered dose while keeping the same anti-diarrhoeal efficacy. Single racecadotril administration induced an anti-diarrhoeal effect with ED50s values of $157.4 \pm 8.5$, $240.0 \pm 6.9$ and $> 300$ mg/kg at 1, 2 and 7 h respectively after injection of endotoxins. Combination of several doses of racecadotril with S. boulardii at 3 g/kg showed a significant reduction of racecadotril ED50s with anti-diarrhoeal values of $58.4 \pm 16.1$ and $104.6 \pm 12.8$ mg/kg at 1 and 2 h respectively, after endotoxins injection. This combination allowed to reduce at least 2 to 3 fold the racecadotril administered dose while keeping the same anti-diarrhoeal efficacy.
**Conclusion:** These results show that combination of S. boulardii CNCM I-745 with loperamide or racecadotril significantly potentiates their anti-diarrhoeal efficacies in the mouse endotoxins-induced diarrhoea model. These compounds interact synergistically through their different mechanisms of action. These findings suggest that these combinations could be effective in the treatment of acute diarrhoea and could reduce loperamide or racecadotril consumption and side effects.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0950 COMBINATION FECAL IMMUNOCHEMICAL TEST AND CLINICAL RISK SCORES TO PRIORITIZE SCREENING COLONOSCOPY: A MULTICENTER STUDY IN THAILAND

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**Introduction:** Fecal immunochemical test (FIT) is the preferred strategy for colorectal cancer screening. In limited-resource countries, there are few well-trained endoscopists, which is incomparable with the screening colonoscopy volume. (Table 1) The Asia-Pacific Colorectal Screening system (APCS) score based on simple clinical risk factors has been developed and validated. Score 4–7 is defined as high risk. FIT and APCS have been individually shown to predict the risk of colorectal neoplasm.

**Abstract No: P0951**

**Table 1:** Different aspects of GI training in evaluated countries

| Country of training (N° of participants) | Length of postgraduate training (years) | Average number of total diagnostic procedures performed [Mean ± SD] | | | | Trainees performing interventional endoscopic procedures (%) | | | | | Trainees very or fully confident in each field at the end of training (%) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Upper endoscopy | Colonoscopy | ERCP | EUS | >30 Hemostatic procedures for non-variceal bleeding | >30 Hemostatic procedurs for variceal bleeding | >50 polipectomy procedures | >10 EMR procedures | >30 PEG placements | Ward clinical activities | Outpatient clinic activities | Luminal endoscopy | Ultrasound | ERCP | EUS |
| Belgium (9)* | 3 | 1217 ± 743 | 638 ± 468 | 17 ± ± 28 | 0 ± 1 | 22.2 | 0 | 100 | 11.1 | 55.6 | 55.6 | 55.6 | 44.4 | 22.2 | 0 | 0 |
| Croatia (8)* | 2 | 1363 ± 630 | 688 ± 285 | 19 ± 45 | 8 ± 17 | 100 | 62.5 | 100 | 62.5 | 50 | 87.5 | 87.5 | 87.5 | 75 | 12.5 | 12.5 |
| Denmark (13)* | 5 | 492 ± 516 | 176 ± 126 | 0 | 0 | 15.4 | 7.7 | 15.4 | 0 | 0 | 84.6 | 84.6 | 75.9 | 7.7 | 0 | 0 |
| France (14)* | 4 | 358 ± 184 | 175 ± 116 | 8 ± 28 | 33 ± 45 | 23.1 | 7.7 | 7.7 | 69.2 | 46.2 | 46.2 | 46.2 | 30.8 | 0 | 0 | 7.7 |
| Germany (10)* | 6 | 900 ± 673 | 430 ± 309 | 55 ± 58 | 125 ± 176 | 70 | 40 | 60 | 20 | 70 | 90 | 90 | 70 | 90 | 0 | 20 |
| Greece (1) | 4 | 3000 | 1200 | 250 | 0 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 0 | 100 | 0 |
| Italy (28)* | 4/5** | 510 ± 369 | 491 ± 401 | 46 ± 125 | 72 ± 151 | 17.2 | 13.8 | 20.7 | 31 | 17.2 | 44.8 | 72.4 | 69 | 34.5 | 6.9 | 6.9 |
| Lithuania (4) | 4 | 109 ± 56 | 78 ± 39 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 50 | 25 | 75 | 50 | 0 | 0 |
| Netherlands (11)* | 6 | 880 ± 378 | 705 ± 235 | 52 ± 46 | 53 ± 50 | 27.3 | 0 | 90.9 | 72.7 | 45.5 | 100 | 90.9 | 90.9 | 0 | 9.1 | 0 |
| Poland (1) | 2 | 50 | 150 | 0 | 0 | 0 | 0 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Portugal (23)* | 5 | 1340 ± 483 | 1002 ± 318 | 79 ± 60 | 162 ± 184 | 91.7 | 58.3 | 95.8 | 95.8 | 79.2 | 95.8 | 87.5 | 91.7 | 29.2 | 8.3 | 37.5 |
| Romania (7) | 4 | 261 ± 88 | 104 ± 54 | 23 ± 56 | 0 | 85.7 | 57.1 | 0 | 14.3 | 14.3 | 57.1 | 28.6 | 28.6 | 57.1 | 14.3 | 0 |
| Russia (1) | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Serbia (1) | 5 | 90 ± 0 | 20 ± 0 | 0 | 0 | 100 | 0 | 0 | 0 | 0 | 100 | 100 | 0 | 0 | 0 | 0 |
| Sweden (3)* | 7 | 183 ± 126 | 67 ± 29 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 100 | 100 | 33.3 | 0 | 0 | 0 |
| UK (10)* | 5 | 1115 ± 750 | 660 ± 675 | 39 ± 63 | 20 ± 63 | 70 | 60 | 70 | 80 | 90 | 90 | 90 | 70 | 0 | 10 | 0 |

*Participants identified through national societies of GI trainees/young gastroenterologists;
**Duration changed 2 years ago

**Table 1:** Asia-Pacific colorectal screening system score

| Clinical risk factors | Criteria | Points |
|---|---|---|
| Age | below 50 years | 0 |
| | 50–70 years | 2 |
| | above 70 years | 3 |
| Gender | Female | 0 |
| | Male | 1 |
| Family history of colon cancer in the first degree relative | Absent | 0 |
| | Present | 2 |
| Smoking | Never | 0 |
| | Current/ past | 1 |

**Aims & Methods:** We aimed to determine the value of the combination of FIT and APCS score in stratifying asymptomatic subjects for screening colonoscopy. We conducted a multicenter study from 6 university hospitals in Thailand between October 2013 and February 2016. Asymptomatic subjects with aged 50–75 years, who participated in a health promotion program, were recruited. All subjects were evaluated for APCS score. FIT was done within 3 days prior to colonoscopy. Quantitative FIT with cut-off hemoglobin of 100 ng/dl was referred as positive. Subjects were divided into 4 groups according to the FIT and APCS results; group I = positive FIT with high risk, group II = positive FIT with non-high risk, group III = negative FIT with high risk, group IV = negative FIT with non-high risk. All underwent colonoscopy and adenoma detection rates (ADRs), advanced ADRs, and cancer detection rates (CDRs) were compared among the 4 groups. The results of FIT and APCS score were blinded to the performing endoscopists.
**Results:** A total of 1,120 subjects (mean age $60.5 \pm 7.1$yrs, female = 62%) were enrolled. The detection rate of adenomas, advanced adenoma, and cancer were 409(37%), 86(8%) and 7(0.6%) respectively. Regarding APCS score, 338 (30%) and 782(70%) subjects were classified as high risk, non-high risk, respectively. Advanced ADR was significantly higher in high risk subjects than in non-high risk subjects (10.4% vs. 6.5%, $p < 0.05$) There were 78(7%) subjects with positive FIT. Subjects with positive FIT had a significantly high advanced ADR compared to subjects with negative FIT (23% vs. 6.5%, $p < 0.001$). In combination of FIT and APCS, 30(2.7%), 49(4.4%), 308(27.5%) and 733(65%) subjects were stratified into group I, II, III and IV, respectively. There were significant differences of ADR and advanced ADR among 4 groups ($p < 0.001$). ADRs were 67%, 59%, 40% and 32% in group I, II, III and IV, respectively ($p < 0.001$). Group I had significantly higher advanced ADR (30%) than group II (22%), group III (8.4%) and group IV (5.5%), ($p < 0.001$).
**Conclusion:** The use of a combination of clinical risk scores and FIT is helpful to prioritize screening colonoscopy. Subjects with positive FIT with high-risk scores should be the first group undergoing for colonoscopy. However, a cost-effectiveness analysis is needed to evaluate the benefit of offering colonoscopy for the rest.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0951 DIFFERENCES AND SIMILARITIES OF GASTROENTEROLOGY TRAINING ACROSS EUROPE: A WEB-BASED, INTERNATIONAL SURVEY

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**Introduction:** There is currently no universal European training program in Gastroenterology and Hepatology. The European Board of Gastroenterology and Hepatology (EBGH) have produced guidance[1] regarding expected competences for European Gastroenterology (GI) trainees but it is unclear as to whether these have been incorporated national curricula. The last evaluation of gastroenterology training across Europe dates back to 2002. [2]
**Aims & Methods:** Our aim was to update the picture of gastroenterology training across Europe to identify differences and similarities between current programs. We developed a web-based 90-point questionnaire composed of 5 sections to investigate different aspects of gastroenterology training including: institutional rules, clinical activities, endoscopy, ultrasound, academic activities including scientific research, financial/socio-economic/employment issues and pitfalls of training programs. Physicians in their last year of GI training or who had recently finished their training, from 16 European countries (Belgium, Croatia, Denmark, France, Germany, Greece, Italy, Lithuania, Netherlands, Poland, Portugal, Romania, Russia, Serbia, Sweden, UK), were invited to participate in the survey. In 10/16 (62%) countries, physicians were identified through national societies of GI trainees/young gastroenterologists.
**Results:** A total of 143 physicians answered the survey (last-year trainees 33%, newly graduated gastroenterologists 77%). Overall, major differences in several aspects of training were identified among all evaluated countries, including access to postgraduate training (local or national application) and its duration (Table 1). Trainees undertake a final exam to complete their training in 11/16 (69%) countries. A minimum number of procedures is required to graduate in 9/16 (56%) countries. Overall European trainees dedicate a median of 12 months of their training period to endoscopy (Interquartile range – IQR: 6–25) but only a median of 3 months (IQR 0–6) to ultrasound training. The actual workload of trainees is usually higher than that forecast by training programmes and up to 13% of trainees complete their training without the supervision of a mentor. Overall, 70–89% of trainees performed a total number of diagnostic endoscopic procedures that fulfills the requirements of EBGH. However, large differences were found between and within countries, especially for interventional procedures (Table 1). Only 52% of trainees have access to pancreatobiliary endoscopy during their training. More than 30% of trainees attend few (<10) academic lessons/year. Approximately 48% of trainees do not receive reimbursement for congress-related expenses. Nearly 66% of trainees dedicate ≤10 hours/month to scientific research, and 80% of trainees undertake research during their free time. Average monthly salaries range from 1200–5200€ which differs considerably among Countries. In 12/16 (75%) countries trainees are paid for night duties and maternity leave. Only a minority of trainees percieve that they are very or fully confident in several GI activities (Table 1). Finally, 86% of trainees believe that GI educational programs should be homogenised across Europe.
**Conclusion:** In this large survey of senior trainees and newly graduated gastroenterologists, considerable differences in several aspects of GI training programs were found both between and within 16 European countries. Nevertheless, there has been some improvement in convergence and adherence to EBGH requirements since 2002.[2] Practical training in ultrasound and interventional endoscopy appear to be still insufficient in most countries. In addition there are significant discrepancies between research opportunities and activities, and support for trainees. Such dissimilarities may lead to disparities in quality of training and, consequently, of healthcare across countries. A higher homogenisation of educational programs and training opportunities across Europe is, therefore, strongly desirable.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0952 RANDOMISED CLINICAL TRIAL: 1-DAY BOWEL PREPARATION VS 2-DAY BOWEL PREPARATION WITH POLYETHYLENE GLYCOL 3350 – A CONTROLLED STUDY OF EFFICACY IN CHILDREN BOWEL PREPARATION FOR COLONOSCOPY

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**Introduction:** Colonoscopy is considered the standard of care for investigating large-bowel and terminal-ileum disease in teenagers and children. The diagnostic accuracy of colonoscopy requires thorough visualization of the colonic mucosa, making bowel preparation a vital element of the procedure. The PEG has showed an option of more secure and more efficacy in the bowel prepare to teenagers and children above two years old. Although there is not gold standard for bowel prepare.
**Aims & Methods:** This study aims to evaluate the effectiveness of PEG 3350 for colonoscopy colon preparation in children and teenagers, considering the measures as followed: full-dose and split-dose. It was conducted as a prospective, randomized controlled trial with children aged 2–18 years undergoing elective colonoscopy. Patients were randomly assigned to receive PEG 3350 for either one (full dose) or two (split dose) days. Children with known fecal impaction, metabolic, cardiac or renal disease were excluded. Subjects reported the tolerability and side effects of PEG 3350 via a survey. Effectiveness of the bowel preparation was assessed using a two bowel cleansing scale during colonoscopy.
**Results:** 52 patients were evaluated aged 02–18 and were scheduled for colonoscopy at the Brasilia Jose Alencar Children's Hospital from November 2014 to October 2015 and were divided into two groups: A) Full-dose with 26 patients and B) Split-dose with 26 patients. The full dose preparation had a success rate of 61.5% and with preparation of Split dose achieved in 92.3% success rate, with statistical significance ($p < 0.0187$) among compared groups. Adverse symptoms in the colon preparation using full dose achieved 11.5% rate of patients and in the case of Split dose it had have a 19.2% rate of patients

**Table Abstract No: P0954**

| Device storage temperature Collection Picker/HM-JACKarc | % difference of Hb concentration 1–7 days OC-SENSOR Autosampling Bottle 3/ PLEDIA | FOB Gold/ SentiFIT 270 | Extel Hemo Auto-MC | |
|---|---|---|---|---|
| | **n** | 12 | 10* | 10* |
| **19°C** | **Average** | 6.4 | −10.1 | −4.8 |
| | **Min** | −35.4 | −19.5 | −19.4 |
| | **Max** | 18.7 | −2.2 | 8.9 |
| **30°C** | **Average** | −31.2 | −32.8 | −22.5 |
| | **Min** | −92.4 | −60.7 | −48.4 |
| | **Max** | 45.0 | −15.8 | 7.7 |

*Two samples gave results below the analytical range.

with no statistical significance if we compare the two groups ($p < 0.703$), and without presenting severe symptoms.
**Conclusion:** This current comparative study was conduct at the Brasilia Jose Alencar Children's Hospital showing a statistical superiority of using of PEG 3350 in two days compared with a only one day. It is important to comment that the colon preparation of two days was effective and secure indicating to be a gold standard for bowel preparation in children and teenagers. There was difference between protocols was observed, the 2 d protocol was superior. Side effects were minimal. Allowing to establish bowel preparation colonoscopy, safe and effective for children and adolescents.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P0953 THE BURDEN OF GASTROINTESTINAL MORBIDITY AND HEALTH RESOURCE UTILIZATION IN YOUNG ADULTS


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**Introduction:** The reported burden of gastrointestinal (GI) morbidity in the Western world is extensive, and close to 20% of the general population is affected annually. The reported burden of GI morbidity in Israel is unknown.
**Aims & Methods:** Aim: To examine the prevalence of GI reported symptomatology, morbidity and utilization of health system resources in a cohort of young adults.
Methods: The study population included all young adults (18–26 years old) who served in the IDF between the years 2005–2015. Comprehensive data regarding their GI-related symptoms, diseases, emergency department visits and diagnostic procedures were obtained from medical records in order to estimate the burden of GI-related morbidity. Summary statistics and frequencies were recorded.
**Results:** A total of 824,476 young adults (38.9% females) were included in the study. During an average follow-up of 2.3 years, 44.2% had at least one GI-related symptom (682 recorded symptoms per 1000 follow-up years) and 48.3% were diagnosed with at least one GI-related disease (656 recorded diseases per 1000 follow-up years). The most common symptoms were abdominal pain, diarrhea, nausea and vomiting, dyspepsia and anemia and nutritional deficiencies (275, 101, 83, 74 and 63 per 1000 follow-up years, respectively). The most common diagnosed diseases were GI-related infections, small intestine disorders (e.g. Celiac), perianal problems, liver-related diagnoses and irritable bowel syndrome (272, 169, 76, 25 and 24 per 1000 follow-up years, respectively). Precancerous conditions and cancer were rare (0.61 per 1000 follow-up years). The emergency room referral rate was 5.5% (37 visits per 1000 follow-up years). Endoscopic procedures were performed in 1.8% (13.5 endoscopies per 1000 follow-up years) and 0.4% had a radiologic exam (3 per 1000 follow-up years).
**Conclusion:** GI diseases are a source of substantial morbidity and utilization of health resources in young Israeli adults
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P0954 FIT SAMPLE STABILITY FOR HAEMOGLOBIN-POSITIVE FAECES USING THREE ANALYSIS SYSTEMS OVER SEVEN DAYS


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**Introduction:** Automated quantitative faecal immunochemical test (FIT) for haemoglobin (Hb) systems include a faecal sampling device (with preservative buffer), laboratory analyser and reagent kit. In colorectal cancer screening programmes faecal samples are usually collected at home and posted back to the laboratory for testing. Samples can be in transit for several days and subjected to a variety of temperatures.
**Aims & Methods:** We investigated the likely effect of sample return time on Hb concentration using naturally Hb-positive faeces stored for seven days at 19°C or 30°C and analysed on three different FIT systems. Twelve Hb-positive samples were taken from stools provided for calprotectin analysis and mixed for two minutes using wooden sticks. Two FIT sampling devices for each of the three FIT systems (Extel Hemo Auto-MC Collection Picker (Kyowa Medex Co. Ltd), FOB Gold (Sentinel Diagnostics), and OC-SENSOR Autosampling Bottle 3 (Eiken Chemical Co.)), were loaded with faeces from the twelve samples. After mixing and incubation for 24 hours at room temperature, Hb was measured using the HM-JACKarc, SentiFIT 270 and OC-SENSOR PLEDIA analysers, respectively. One of the sampling devices for each sample was then stored in the dark at room temperature (15–23°C) for seven days and one stored in the dark at 30°C for seven days. After mixing the samples, Hb was re-measured on days 3, 5 and 7. The samples stored at 30°C were allowed to cool to room temperature before analysis.
**Results:** The average percentage difference between the Hb concentration on day 1 and day 7 was calculated for each FIT system. The minimum and maximum percentage differences were also calculated.
**Conclusion:** Faecal samples that were positive for Hb collected and stored in the OC-SENSOR Autosampling Bottle 3 devices showed the lowest average percentage change over seven days at 19°C (negative percentage difference), followed by the FOB Gold device (positive percentage difference) and the Extel Hemo Auto-MC Collection Picker (negative percentage difference). At 30°C OC-SENSOR Autosampling Bottle 3 devices gave the lowest average percentage change over seven days, followed by the FOB Gold device and the Extel Hemo Auto-MC Collection Picker. All three devices showed negative average percentage differences at 30°C.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0955 REFERRALS TO A TERTIARY HOSPITAL: A CLINICAL SNAPSHOT OF PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS AND EFFECTIVENESS OF PRIMARY CARE MANAGEMENT

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**Introduction:** Although current guidelines recommend that functional gastrointestinal disorders (FGID) can be effectively diagnosed and managed in primary care [1] tertiary care referrals exceed capacity.

**Aims & Methods:** This study aimed to utilise referrals to tertiary care as a window to the effectiveness of FGID management in primary care in Australia. Consecutive patients with likely FGID referred to one gastroenterology outpatient department (2013–2015) were invited to participate in a RCT of a novel care pathway. Patients completed an intake survey and a standard panel of screening tests. Referral quality was assessed with content analysis, and general practitioners (GP) surveyed to explore referral reasons.

**Results:** 111 patients (64% female, mean 42 [SD 15] y) responded; 90 intervention, 21 waitlist control. 60% were tertiary educated and 61% employed. Symptom duration was >2 y (64%) and 44% reported psychological co-morbidities. 52% experienced persistent/distressing symptoms with reduced daily functioning in 17% of these. 66% had never seen a gastroenterologist, yet 18% had previously consulted more than once. 37% had consulted their GP in the last 4 weeks for these symptoms and 87% were using at least one treatment (medications, 35% prescription, 36% over the counter,17% complementary and alternative; 23% diet; 32% >1 treatment type) with little/no improvement in 69%. 40% were dissatisfied and 36% only partially satisfied with management (Table 1). Dissatisfaction was related to both the lack of provision of a diagnosis (70%) and effective treatment options ($p < .001$ for each). Treatment costs in the previous 4 weeks varied between $0 (in a third) and $1300. Table 1. Range of statements made by patients regarding dissatisfaction with management.

"(GP) has offered no assistance, has told me I need to learn to live with it" Pt 99
"Have no diagnosis, nor any idea how to treat it" Pt 106
"I've seen different GP's and at this stage, all they have been able to offer me are various tests. This has been going on for a few years" Pt 29
"No results, constant hand balling. Ultimately no relief and now on a 12 month waiting list for the next step" Pt 85
"I don't have medicine to fix the problem. I'm not sure what the doctors think about my problems. I'm not getting much explanations. Looks all my problems is an enigma" Pt 73

Referrals lacked information required for safe triage such as age (49%), gender (27%), symptom duration (50%) and clinical alarms (71%). GPs underreported alarms (13% GPs vs 86% patients) with 34/90 patients subsequently receiving prompt GE review after screening, due to a change in triage category. 61 GPs completed the survey. Reasons for referral were repeat presentations (n = 32), diagnostic uncertainty (n = 19), to ensure nothing is missed (n = 19), patient request (n = 17), treatment failure (n = 16) and patient fears (n = 14). 28 GPs were confident their patient had a FGID yet referred for confirmation (n = 24) and treatment advice (n = 4). 20 were "unsure", 7 "not confident" and 5 confident in an alternate diagnosis (3 unable to suggest what this was).

**Conclusion:** This window into primary care management of patients with likely FGID indicates that the majority of patients have long-term, distressing symptoms and yet have not received a diagnosis (70%) or previously seen a gastroenterologist (66%); although a third seek repeat specialist consultation. These data suggest that GPs lack confidence in diagnosing and managing FGID and we propose that education and structured support tools may be an effective strategy to facilitate primary care management of FGID.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0956 GP PARTICIPATION IN INCREASING UPTAKE IN BOWEL CANCER SCREENING: THE PEARL PROJECT

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**Introduction:** Uptake of bowel cancer screening in England is about 56%, a figure that has changed little since the programme began in 2006. The NHS Bowel Cancer Screening Programme (BCSP) in England is organised centrally, without the direct involvement of general practitioners (GPs). There is however evidence to suggest that people are more likely to be screened if they are encouraged to do so by their GP. The Practice Endorsed Additional Reminder Letter (PEARL) project is a collaboration between the BCSP Southern Hub and a group of Wessex GPs working for Macmillan Cancer Support in partnership with the Wessex Strategic Clinical Network.

**Aims & Methods:** Wessex practices with BCSP uptake below 55% (prevalent episodes 2008–2013) were invited to participate. Between September 2014 and October 2015, subjects registered with participating practices who had not returned a test kit within 30 days of a standard reminder letter were identified on the BCSP database and their GPs asked to identify those who should not be sent a further reminder (end-of-life-care etc.). The Hub then confirmed that GP-included subjects remained non-respondent and a second reminder letter was sent out with the appropriate GP letterhead and signature. 25 non-PEARL practices were selected, matched to the 25 PEARL-registered practices by previous prevalent participation rates and number of invitees. Comparison of uptake in these two groups was performed using Mantel-Haenszel estimation conditioning, producing relative risk and 95% confidence intervals.

**Results:** The intervention significantly increased the probablillity of uptake by 4% in absolute terms from 50% to 54%, a proportional increase of 8% (RR = 1.08, 95% CI 1.05–1.11, $p < 0.001$). Restricting analysis to subjects who had not completed a kit by the index date (date PEARL reminder letter was sent, or would have been sent if in a participating practice), also showed that the intervention had a significant effect (RR = 2.96 [2.37–3.69]).

**Conclusion:** The PEARL intervention significantly increased uptake both as a proportion of all invitees or only those invitees who had not completed a kit by the index date. The extra work required at the Hub and practices will be evaluated and recommendations made about the viability of rolling this process out nationally within the BCSP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0957 POST-POLYPECTOMY BLEEDING AMONGST PARTICIPANTS OF NEW ZEALAND BOWEL SCREENING PILOT PROGRAMME

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**Introduction:** The New Zealand Bowel Screening Pilot (NZBSP) Programme was implemented from year 2012 to 2015. Subjects aged 50 to 74 eligible for publicly funded healthcare from Waitemata District Health Board area were invited to participate in the programme.

**Aims & Methods:** To evaluate post-polypectomy bleeding (PPB) complications in NZBSP Programme. Demographics, polyp characteristics, polypectomy techniques, PPB clinical parameters, resource utilisation and management outcomes were analysed.

**Results:** Of 7643 participants who underwent colonoscopy under NZBSP Programme, 53 presented with PPB over the four-year period, overall PPB rate was 0.7%. PPB rate was highest in first year at 1.5%, with rates of 0.4%, 0.4% and 0.6% noted over each consecutive year. Antithrombotic agents were managed per local guidelines prior to these colonoscopy, including Clopidogrel (n = 3), Warfarin (n = 5, 3 had bridging Enoxaparin) and Dabigatran (n = 3). Median polypectomy rate was 3 polyps per participant. Median size of largest polyp resection was 12 mm (range 3–50 mm), 15 of these were 20 mm or larger, 24 were located in right colon. Hot snare method was employed in 91%, 8/48 (17%) were piecemeal endoscopic mucosal resections. 12 patients had early PPB (intra-procedural and up to 24 hours), median interval to onset of PPB was 2 days (range 0–16). Median hospital stay was 2 days (range 0–34), 16 patients (30% PPB cases, 0.2% overall participants) received red blood cell transfusions, 2 required additional blood products. Computed tomography angiography was performed in 3 patients, of these 1 proceeded to embolisation and 2 had repeat endoscopy; computed tomography of abdomen was performed in another participant. Repeat endoscopy rate was 17% (5 colonoscopies and 4 flexible sigmoidoscopies): endoscopic therapies were applied in 7 procedures, 1 polypectomy ulcer required no therapy and 1 had proximal bleeding and proceeded to surgery. Surgical management rate of PPB was 7.5% (3 right hemicolectomies and 1 Hartmann's procedure).

**Conclusion:** The NZBSP Programme has similar polypectomy-related bleeding rate when compared to other larger series bowel cancer screening programme[1].

**Disclosure of Interest:** P. Frankish: Lead Endoscopist Bowel Screening Pilot, Waitemata District Health Board, Auckland
All other authors have declared no conflicts of interest.

**Table Abstract No: P0959**

Mean TPS for referrals with checklists compared with referrals without checklists.

| Clinical case | N referrals | With referrals (mean TPS, 95% CI) | Withouth checklists(mean TPS, 95% CI) | P* |
|---|---|---|---|---|
| Dyspepsia | 22 | 22.8 (20.8–24.8) | 12.8 (11.1–14.5) | <0.001 |
| Change of bowel habit | 22 | 24.1 (22.3–25.8) | 15.8 (13.0–18.7) | <0.001 |
| Diarrhoea | 23 | 21.8 (19.8–23.9) | 15.2 (12.7–17.8) | <0.001 |
| Rectal bleeding | 24 | 25.3 (23.6–26.9) | 17.7 (15.3–20.1) | <0.001 |
| Abdominal pain | 20 | 19.6 (17.1–22.1) | 16.3 (13.3–19.2) | 0.029 |
| Constipation | 21 | 18.6 (17.1–20.1) | 13.9 (11.1–16.6) | 0.001 |
| Dyspepsi | 21 | 22.5 (19.5–25.5) | 14.3 (12.2–16.5) | <0.001 |
| Elevated liver enzymes/jaundice | 20 | 21.5 (19.3–23.7) | 17.5 (14.6–20.4) | 0.007 |
| Total | 173 | 22.1 (21.3–22.9) | 15.4 (14.6–16.3) | <0.001 |

*paired sample t-test

#### Reference

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### P0959 THE IDRI STUDY: EFFECT OF DYNAMIC, DIAGNOSE SPECIFIC CHECKLISTS ON REFERRAL QUALITY IN GASTROENTEROLOGY- A RANDOMIZED CROSS-OVER STUDY

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**Introduction:** The quality of referral letters in gastroenterology is variable, with a significant proportion of low quality. This is a challenge for consultants assessing referral letters and prioritizing the patients for appropriate examinations/consultations. Some studies have shown effect of checklists on referral quality, but none has examined this in a standardized setting.

**Aims & Methods:** The aim of the study was to assess the effect of dynamic, diagnose specific interactive checklists on the quality of GPs' referral letters. In order to reduce confounding by organizational- or patient- variation the assessment was performed in a standardized setting. An Electronic Patient Record (EPR) simulator was developed, and 8 patient cases were made using the most common reasons for referral from the National Prioritization Guideline in gastroenterology. The patient cases were incorporated in the EPR-simulator, allowing doctors to chat with the virtual patients to obtain a medical history and results from relevant examinations and work-up. From April 2014 to October 2014, 45 GPs were invited to perform virtual consultations and randomized to generate referral letters either by using dynamic, diagnose-specific check list or a free text format. After an interval of 3–12 months, the GPs repeated the process in a cross-over design with the opposite referral- type. Referrals were assessed using a Thirty Point Score (TPS) for referral quality.

**Results:** From April 2014 to July 2015, 25 GPs completed both rounds of the study. Participating GPs were an average of 52.3(range 33–63) years old, 60 %female. Average TPS was 22.1(21.3–22.9) in the checklist-group and 15.4(14.6–16.3) in the free-text group($p < 0.001$). Individual TPS for each indication is shown in the table.

**Conclusion:** The results from this study indicate that there is a considerable positive effect of check-lists on referral quality in gastroenterology. These results are most likely valid also for other medical specialties.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00

## OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS II – POSTER EXHIBITION

### P0960 DELPHI STUDY ON THE MANAGEMENT OF IRON DEFICIENCY ANAEMIA IN PATIENTS WITH GASTROINTESTINAL BLEEDING

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**Introduction:** Gastrointestinal bleeding is the commonest cause of iron deficiency anaemia (IDA). Guidelines on the management of IDA due to GI bleeding are outdated and lack information on the use of high-dose IV iron formulations in this context.

**Aims & Methods:** Aim: To gain expert consensus on the optimal management of GI bleeding associated IDA. Methods: An e-Delphi study was conducted among 27 European experts in gastroenterology and IDA (senior academics and senior clinicians from 7 European countries) under the direction of a study chairman and steering group. The experts completed a non-directive narrative questionnaire about their clinical practice and opinions on the optimum management of IDA due to GI bleeding, including the place of high dose IV iron formulations in iron replacement therapy. Narrative questionnaire results were analysed to identify unique propositions about the optimal management of IDA due to GI bleeding. The resulting pool of propositions was used to formulate a Delphi questionnaire with 126 propositions, focussing on those most relevant to the study aim. The Delphi questionnaire was completed on-line by the 27 experts using the Delphi Process Research Unit e-portal. Analysis determined the level of agreement between the 27 experts on each of the 126 propositions. If there was at least 75% agreement on the correctness of a proposition, it was considered to be supported by a consensus. Free text comments were listed and subjected to qualitative analysis.

**Results:** There was a consensus in support for 53 of the 126 propositions tested. Five important themes were identified: 1/ There is a need for new guidelines on the management of IDA in patients with GI bleeding, including practical advice for non-specialists and the identification of "Red Flags" for iron replacement therapy. 2/ Choice of iron formulation to treat IDA in GI bleeding should be based on clinical considerations (primary GI disorder, pathophysiology, presence of inflammation, presence of comorbidity and malabsorption). 3/ Use of blood test threshold values is not a sufficient basis for determining the most appropriate type of iron therapy to use (high dose IV or traditional oral). 4/ Oral iron therapy is not always an appropriate first line treatment in cases of IDA due to GI bleeding. 5/ Timely iron supplementation can reduce the need for blood transfusion.

**Conclusion:** Our study suggests that the current use of IV iron by experts in the field is driven by clinical considerations rather than by target laboratory test results or treat/no-treat thresholds. The use of high dose IV iron formulations is logical because compliance is certain, the onset of beneficial effects is fast, the formulations are well tolerated and efficient to use, as shown by evidence from RCTs. New guidance is needed on the optimal management of IDA in patients with GI bleeding including advice on the use of high-dose IV formulations of iron.

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## P0961 URGENT ENDOSCOPY FOR NONVARICEAL UPPER GASTROINTESTINAL HAEMORRHAGE: IMPACT OF OUT-OR-HOURS PRESENTATION AND TIMING OF ENDOSCOPY

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**Introduction:** Acute nonvariceal upper gastrointestinal haemorrhage (ANVUGIH) is a common condition with significant associated morbidity and mortality. Although performance of endoscopic haemostasis improves the outcomes, evidence sustaining benefits for very early endoscopy is scarce.
**Aims & Methods:** Our aims were to evaluate the impact of out-of-hours presentation and the timing of endoscopy on the outcomes of patients presenting with ANVUGIH to the emergency department. We performed a retrospective analysis of consecutive patients undergoing upper gastrointestinal endoscopy (UGIE) due to ANVUGIH between January 2010 and June 2013 in our centre. Inpatients were excluded. Timing of UGIE (first 6 hours, 6 to 12 hours or later than 12 hours after admission) and daytime (8–20 h) versus out-of-hours (20–8 h) presentation were compared for mortality, need for urgent surgery and rebleeding.
**Results:** From January 2010 to June 2013 there were 453 episodes of ANVUGIH (64% males, mean age 66.4 years). Slightly more than half (55%) of UGIE were performed out-of-hours, 34% in the first 6 hours after admission and 36% between 6 and 12 hours after admission. Global 30-day mortality rate was 6.2%. No predictors of outcomes were found for daytime ANVUGIH. For out-of-hours ANVUGIH, haemoglobin less than 7 g/dL was an independent predictor of in-hospital and 30-day need for urgent surgery, rebleeding and mortality; Rockall score >7 predicted in-hospital and 30-day mortality and personal history of neoplasia predicted 30-day mortality. Patients presenting with out-of-hours ANVUGIH were more likely to undergo endoscopic haemostasis. Timing of UGIE was not a predictor of mortality or other outcomes.
**Conclusion:** Endoscopy during the first 6 hours after admission did not improve mortality, rebleeding and the need for surgery. In out-of-hours ANVUGIH, highly qualified care should be provided for patients with higher Rockall score and lower haemoglobin levels.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0962 A COMPARATIVE STUDY OF RISK ASSESSMENT SCORES FOR ACUTE UPPER GI BLEEDS, IN PREDICTING NEED & TIME FOR INTERVENTION

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**Introduction:** While managing patients with acute upper GI bleed (AUGIB) a simple numerical score can be helpful to identify high risk groups & need for intervention as recommended by NICE. Recent NCEPOD report for AUGIB reported that only 32% patients had a Pre-endoscopy risk assessment performed. Two commonly used scoring systems in UK are GBS (Glasgow Blatchford score) and RCS (Rockall score). Recent comparisons have shown that the GBS was superior in identifying need for hospital-based intervention1 while RCS was better in predicting mortality.2
**Aims & Methods:** We conducted a retrospective study of 893 patients, admitted to the hospital and treated in endoscopy unit of Cardiff & Vale health board between September 2010 to September 2013 with AUGIB. We calculated the GBS and pre & post endoscopy RCS for each and compared several outcomes.
**Results:**

Time to scope vs outcome in Patients with GBS >10 (High risk)

| Hours to OGD | Total | Ther Intervention | Died |
|---|---|---|---|
| >24Hrs | 240 | 61(25.4%) | 45(18.75%) |
| 6–24Hrs | 108 | 52(48.1%) | 8(7.4%) |
| <6 hrs | 14 | 8(57.14%) | 4(28%) |

Overall, GI bleed related mortality was only 3.1% in our study, with chronic liver disease being one of the main risk factor. GBS was superior in identifying patients suitable for safe discharge with outpatient management. The GBS was also better at predicting the need for endoscopic intervention. Our study also found that very early endoscopy (ie <6 hours) compared to rapid endoscopy (6–24 hours), did not improve survival in the highest risk patients (ie GBS>10), and in fact had a significantly worse mortality rate of 28% versus 7.4%.
**Conclusion:** The GBS score is superior to the pre-endoscopy Rockall in rationalising need & timeliness of intervention. The post-Rockall score is shown to be the better predictor of mortality. This study also reinforced the importance of access to rapid endoscopic intervention within 24 hours, but did not demonstrate the need for very early gastroscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0963 MALLORY-WEISS SYNDROME: NOT SO GOOD NEWS

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**Introduction:** Mallory-Weiss syndrome (MWS) is a frequent cause of upper gastrointestinal bleeding (UGIB). Although classically considered mild and self-limited, recent evidence suggests that mortality can be substantial.
**Aims & Methods:** In this study we aimed to analyse the prevalence, patient characteristics, endoscopic treatment and main outcomes of patients admitted for MWS and to compare them to those of peptic ulcer bleeding. We performed a retrospective single-centre cohort of consecutive patients with upper non-variceal gastrointestinal bleeding due to all causes between January 2010 and June 2013. Patient demographic characteristics, endoscopic variables and outcome parameters, including rates of haemostasis, recurrent bleeding, surgery and mortality were analysed. Comparative analysis was performed between MWS and peptic ulcer bleeding.
**Results:** Seventy-two patients with UGIB due to MWS (69.4% male, mean age 61.1years) and 347 with peptic ulcer bleeding (70.0% male, mean age 64.6 years) were evaluated. In the MWS cohort, hematemesis was the commonest form of presentation (88.9%) and almost half of the patients were haemodynamically unstable (45.8% presented tachycardia or hypotension). Endoscopic haemostasis was performed in 40 patients (55.6%; including 19.4% adrenaline injection only, 5.6% hemoclipping only and 29.1% combined therapy) with no immediate complications. 30-day rebleeding, surgery and mortality rates were respectively 2.8 (n=2), 0.0 (n=0) and 2.8% (n=2, only 1 due to rebleeding). No predictors of outcome could be found. When compared with peptic bleeding, MWS patients presented more frequently with hematemesis (91.4% vs 53.9%, p=0.000) and higher haemoglobin (11.3 g/dL vs 8.6 g/dL, p=0.000). The proportion of anticoagulated patients was twice as high (18.8% vs 9.9%, p=0.032). In-hospital and 30-day mortality for all causes (p=0.423 and p=0.244, respectively) or related to bleeding (p=0.303) was similar, despite a trend towards lower mortality due to MWS (2.8% vs 6.1%). Significant differences were noted in relation to lower need for surgery (p=0.012) and rebleeding (p=0.026) in MWS patients.
**Conclusion:** MWS commonly presents as hematemesis and the majority of patients need endoscopic haemostasis due to maintained bleeding. Although rebleeding and surgery rates are lower, mortality is comparable to that of peptic ulcer bleeding, stressing the need for high standard quality care and management.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0964 THE ROLE OF ENDOSCOPIC HEMOSTASIS FOR PERIAMPULLARY DIVERTICULAR BLEEDING

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**Introduction:** Upper gastrointestinal bleeding (UGIB) is gastrointestinal emergency that results in substantial morbidity and mortality. Timely and precise bleeding control after resuscitation is necessary. Endoscopic hemostasis has also continued to evolve. However, endoscopy often fail to visualize the exact focus of bleeding when there is massive bleeding, large amount of bloody debris impairing the endoscopic view, or the location such as periampullary diverticulum is difficult to approach.
**Aims & Methods:** This study is aimed to evaluate the role of endoscopic hemostatic modalities for periampullary diverticular bleeing. There was a lack of data for endoscopic control of periampullary diverticular bleeding because the incidence was low, precise targetting for bleeding focus was difficult. We examined the successful endoscopic hemostasis or other hemostatic modalities such as angioembolization for the periampullary diverticular bleeding. The patients' medical records were retrospectively analyzed during 5 years [Apr. 2011 ~ Mar. 2016] in our hospital.
**Results:** During 5 years, 2,237 cases [1,583 patients: male 1,171 (73.9%), female 412 (26.0%), mean age 61.4 ± 14 years)] were treated with endoscopic hemostasis. 199 cases (8.9%) were lower gastrointestinal hemorrhage and 2,038 cases (91.1%) were upper gastrointestinal hemorrhage (including 654 cases (29.2%) of variceal bleeding). Periampullary diverticular bleedings were happened to 7 patients [male 4, female 3, mean age 80 ± 11 years]. There were 4 Dieulafoy's lesions and 3 ulcerative lesions in periampullary diverticulum. 3 patients were treated with radiologic angioembolization as initial hemostatic modality and 4 patients were treated with endoscopic hemostasis (3 hemoclippings and 1 band ligation). Angioembolization is followed by hemoclipping for 1 patient. 2 of 4 endoscopic hemostasis were done by cap-assisted endoscopy. All 7 patients were recovered without rebleeding.
**Conclusion:** This study was limited by being single center observational study. However, the endoscopic hemostasis for periampullary diverticular bleeding could be considered as alternative to surgery or angioembolization.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0965 AIMS65 SCORE AND GLASGOW BLATCHFORD SCORE SHOW NO DIFFERENCE IN PREDICTING REBLEEDING RATE AND MORTALITY IN VARICEAL BLEEDING

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**Introduction:** To compare the performance of the AIMS65 score and Glasgow Blatchford score (GBS) in predicting specific clinical end-points and the need for blood transfusion in patients with variceal bleeding.
**Aims & Methods:** Between January 2008 and December 2013, we retrospectively analyzed 225 consecutive hospitalized patients managed for endoscopically confirmed UGIB (upper gastrointestinal bleeding). The GBS and AIMS65 score were calculated. Discriminative ability for each score was assessed using the receiver operated characteristics curve(ROC) analysis.
**Results:** A total of 225 patients (mean age 61.3 years), frequently diagnosed with alcoholic cirrhosis(195/86.7%), presented with variceal bleeding during the study period. The overall 30-day hospital mortality rate was 17.3%, rebleeding rate was 9.8%, and median hospital stay was 6(1–35) days. Red blood cell transfusion was required in 171(76%) patients with an average of 3.2 red blood cell transfucion packs. Initial hemostasis was achieved with N-butyl cyanoacrylate (151/79.1%) and endoscopic variceal ligation(40/20.9%). There was no statistically significant difference among AIMS65 score and GBS in predicting mortality [(AUROC 0.70(CI 95% 0.62 to 0.77) vs 0.64(CI 95% 0.55 to 0.71)] or rebleeding rate[AUROC 0.74(CI 95% 0.67 to 0.81) vs 0.60 (CI 95% 0.51 to 0.67).] The GBS was superior in predicting the need for blood transfusion compared to AIMS65 score[AUROC 0.75(CI 95% 0.67 to 0.82) vs 0.61(CI 95% 0.53 to 0.66)].
**Conclusion:** The AIMS65 score and GBS are comparable but not useful for predicting outcome in patients with variceal bleeding. The GBS is superior in predicting the need for transfusion compared to AIMS65 score.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0966 A PHASE III CLINICAL TRIAL TO EVALUATE THE ENDOSCOPIC EFFICACY AND SAFETY OF DA-5204, WITH NEW FORMULATION IN GASTRO-RETENTIVE SYSTEM, IN PATIENTS WITH ACUTE OR CHRONIC GASTRITIS

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**Introduction:** DA-5204 (Stillen 2X®) is a new formulation of DA-9601 (Stillen®) with gastro-retentive system (floating technique) that is in the treatment of acute or chronic gastritis. This technique is improved usage of DA-9601 from t.i.d. to b.i.d.. DA-9601 is a phytopharmaceutical derived from *Artemisia princeps*, which has antioxidative and anti-inflammatory actions.
**Aims & Methods:** The study aimed to evaluate the endoscopic efficacy ratio, endoscopic cure ratio and safety for DA-5204. In this multicenter (21 investigational sites), double-blinded, stratified randomized, active controlled, parallel group, non-inferiority trial, 421 patients with acute or chronic gatritis over a 2-week period were randomly assigned to groups for coincidential treatment with DA-5204 (90 mg, b.i.d.) (209 patients for full analysis) or DA-9601 (60 mg, t.i.d.) (212 patients fo full analysis). The primary endpoint was the endoscopic efficacy ratio (used modified Lanza Score) and the secondary endpoint cure ratio and gastric symptoms (epigastric pain, heartburn, reflux, nausea, vomiting, belching and bloating).
**Results:** At week 2, endoscopic efficacy ratio with DA-5204 and DA-9601 were 42.1% (88/209) and 42.5% (90/212), respectively. The difference between th groups was −9.8%, indicating non-inferiority of DA-5204. In secondary

endpoint, endoscopic cure ratio with DA-5204 and DA-9601 were 37.3% (78/209) and 37.3% (79/212), gastric symptoms were 40.4% (84/209) and 40.8% (86/212), respectively. Finally, adverse event ratio od safety issue were not different in both groups (8.4% vs. 8.8%), significantly. Serious adverse events were not reported in both groups.
**Conclusion:** In evaluation of efficacy and safety, DA-5204 (b.i.d.) was equal to DA-9601 (t.i.d.) in patients with acute or chronic gastritis. We should have to get more data with continuous clinical studies. In addition, we will develop a qd (once a day) formulation through formulation studies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0967 IN-HOSPITAL AND DELAYED MORTALITY IN A SINGLE CENTER SERIES OF UPPER GASTROINTESTINAL BLEEDING, A CRITICAL ANALYSIS

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**Introduction:** Upper gastrointestinal bleeding is a common cause of hospitalization, with an estimated annual incidence ranging from 50 to 150 cases per 100000 people, and with morality rates ranging from 2% to 15% of the admitted patients. Factors found to be predictors of mortality include advanced age, low hemoglobin level, low systolic blood pressure, blood in a gastric aspirate, severe comorbidities (neoplasm, cirrhosis), worsening health status, rebleeding, hypoalbuminemia, elevated creatinine, elevated serum aminotransferase levels, onset of bleeding while inpatient, and active bleeding or other stigmata of recent hemorrhage at the time of endoscopy. However, mortality is not always caused by the gastrointestinal bleeding itself, but by the worsening of previous comorbidities, misbalances in their chronic treatment, or by other disease in which upper GI bleeding is only an intercurrent outcome.
**Aims & Methods:** The aim of this study is analyze inpatient and delayed 6 months mortality in patients with a previous admission because of an upper GI bleeding. This was a prospective cohort study on consecutive patients admitted to the "Virgen de las Nieves" University Hospital emergency room for the management of upper GI hemorrhage over 36 months from January 2013 to January 2016. All patients received upper endoscopy and information regarding patients' demographic data, comorbidities, current medications (including antiplatelet drugs, NSAIDS and oral anticoagulants), clinical presentations, hemodynamics, admission laboratory test results, and endoscopic findings was collected. Interventions were recorded, including the need for blood transfusion and the number of packed red cells units per patient, endoscopic therapy, radiologically guided hemostasis, and surgery. Clinical outcomes documented were in-hospital and delayed 6-months mortality, rebleeding, bleeding persistence.
**Results:** 449 patients were included (304 males; aged $64.32 \pm 16.7$). Presenting symptoms were melena ($n = 309$; 68.8%), hematemesis ($n = 236$; 52.7%), and hematochezia ($n = 43$; 9.6%). Overall in-hospital mortality was 9.8% ($n = 44$) but the GI hemorrhage specific mortality rate was $n = 23$ (5.1%). Among patients who died in the first admission, the main causes were hemorrhagic shock followed by hepatic encephalopathy. Active bleeding was observed in 60%, and 31% presented with esophageal varices, 22% gastric ulcers and 18% duodenal ulcers. Only 6% had neoplasms. In patients with delayed mortality 31% had an active bleeding in the first admission, 34% had esophageal varices, 25% a gastric ulcer but only 9% a duodenal ulcer. Neoplasms were found in 6% of patients. In this group, the leading causes of mortality were neoplasms and variceal bleeding. However, cardiovascular causes of mortality accounted 33% (Table 1). Delayed mortality was related with any type of hemorrhagic events ($p < 0.0001$). Considering most of cardiovascular or hemorrhagic delayed events preventable, we observed that half of the patiens with a delayed mortality ($n = 22$) had a potentially preventable cause (Myocardial infarction (4), stroke (4), bleeding esophageal varices (8), heart failure (3) and gastric ulcer bleeding (3)). Factors related with this mortality were AIMS65 > 2 at admission ($p < 0.0001$; HR: 1.775; 95%CI: 1.166–2.702). Age was not related with risk in our cohort. AIMS65 showed a good prognosis prediction ability regarding delayed preventable deaths (AUC 0.745; 95%CI: 0.642–0.849).

**Table 1:** Cause of delayed (6months) mortality

| | |
|---|---|
| Neoplasms | 11 (25.4%) |
| Variceal bleeding | 8 (17.8%) |
| Myocardial infarction | 6 (13.3%) |
| Heart failure | 5 (11.1%) |
| Stroke | 4 (8.9%) |
| Haemorrhagic shock | 3 (6.7%) |
| Surgical complications | 3 (6.7%) |
| Cirrhosis, encephalopathy | 2 (4.4%) |
| Biliary disease (cholangitis, pancreatitis) | 2 (4.4%) |
| Aspiration pneumonia | 1 (2.2%) |

**Conclusion:** Acute and delayed mortality in upper GI bleeding have different patterns. While cirrhosis complications are important in both groups, especially esophageal varices, advanced neoplasms have an important role in delayed mortality. In this last group of patients, there are a subgroup which mortality could be considered non-malignant or preventable. In patients with no malignancies, AIMS65 was a good predictor of mortality, and could select a subset of patients in which an intensive follow-up and therapy should be established.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0968 ACUTE NECROTIZING ESOPHAGITIS: A RETROSPECTIVE CASE SERIES

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**Introduction:** Acute necrotizing esophagitis (ANE), which presents as a black esophagus on endoscopy, is a rarely described entity. Its incidence has not yet been established, and its multifactorial etiology remains unknown.
**Aims & Methods:** The aim of the study was to establish the incidence, risk factors, clinical presentation, endoscopic features, complications and outcomes of the disease. A retrospective analysis of clinical, laboratory, endoscopic and histological data and the clinical course in 17 patients with acute necrotizing esophagitis was carried out over a 5-year period (from 2010 to 2014).
**Results:** ANE was diagnosed in 17 of 11 023 upper gastrointestinal endoscopies (0.15%) carried out during the 5-year period. The average age of the patients was 77.6 years (range 53–90), with no gender predominance (53% females versus 47% males). 88% of the patients had comorbid conditions, particularly hypertension (59%) and ischemic heart disease (41%). In 86% of cases, ANE became evident with upper gastrointestinal bleeding, without hemodynamic instability in the majority of cases (82%). The lesions predominantly affected the lower two-thirds of the esophagus (65%), and there were coexisting abnormal endoscopic findings in 88% of cases. Hypoalbuminemia was observed in 16 patients (94%) with average values of 2.1 g/dL, reflecting a poor nutritional status. Empirical supportive therapy, including oral nutritional rest, proton pump inhibitors and broad-spectrum antibiotics was provided. Endoscopic remission was documented in 5 cases. Esophageal stricture in one case was the only reported complication. Seven patients (41%) died of other causes (coexisting illnesses).
**Conclusion:** In this series, the prevalence of ANE was 0.15%. It is a serious clinical entity that should be considered in the differential diagnosis of upper gastrointestinal bleeding, particularly in elderly patients. The prognosis depends more on the patient's advanced age and on comorbid illnesses than on the course of the esophageal lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0969 PREDICTION OUTCOME OF ACUTE NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING: PROGNOSTIC VALUE OF NON-INVASIVE RISK ASSESSMENT SCORES

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**Introduction:** Non-variceal gastrointestinal bleeding (NVGB) remains a common and challenge disease for gastroenterologists. Predicting the outcome in the moment of patient admission is crucial in the best management of NVGB.
**Aims & Methods: Aims:** Determine the prognostic value of usual scores used in NVGB, particularly the pre-endoscopic ones. **Methods:** Retrospective case-control study of 121 NVGB. Compared patients with worse prognosis(Group 1), defined by intra-hospital mortality, re-bleeding and hemodynamic instability at presentation; need of endoscopic therapy(Group 2); and early and late (<1 month of index event) refractory to endoscopic therapy(Group 3) with controls. Evaluated clinical and biochemical variables, non-invasive prognostic scores [admission Rockall score(aRS), Glasgow-Blatchford score(GBS), modified Glasgow-Blatchford score(mGBS), AIMS-65] and invasive prognostic scores [total Rockall score(tRS)].
**Results:** Worse prognosis occurred in 47(38.8%) patients with intra-hospital mortality in 13.2%(16/121), 28.9%(35/121) of re-bleeding and hemodynamic instability in 22.3%(27/121). Endoscopy therapy was performed in 70.2%(85/121) of patients with therapeutic refractory in 50 patients (41.3%). Relatively to patients with worse prognosis(Group 1), the prognostic scores had a similar predictive value (AUROC0.632–0.716;$p < 0.015$), being the tRS (AUROC0.716;$p < 0.001$), mGBS (AUROC0.705;$p < 0.001$) and AIMS-65 (AUROC0.688;$p < 0.001$). Patients with endoscopic therapy need(Group 2), the best prognostic scores were tRS (AUROC0.834;$p < 0.001$), mGBS (AUROC0.733;$p < 0.001$) and GBS (AUROC0.725;$p < 0.001$). The prognostic scores AIMS-65 (AUROC0.702;$p < 0.001$), mGBS (AUROC0.696;$p < 0.001$) and tRS (AUROC0.682;$p = 0.001$) showed best accuracy in predicting refractory to endoscopic therapy(Group 3).
**Conclusion:** There are many scores to predicting outcome in NVGB. The non-invasive prediction of worse outcome in NVGB is better defined by mBGS and

AIMS-65 scores. The mGBS is the best prognostic score in selecting patients who needs endoscopy and/or hospital admission.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0970 POPULATION PREVALENCE OF ROME IV AND ROME III FUNCTIONAL DYSPEPSIA IN THE UNITED STATES (US), CANADA AND THE UNITED KINGDOM (UK)

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**Introduction:** The new Rome IV diagnostic criteria for functional dyspepsia (FD) are similar to Rome III except they do away with several qualifiers for diagnosing the Epigastric Pain Syndrome (EPS) variant. It is unknown how the new criteria will affect the prevalence and demographic distribution of FD in the general population.
**Aims & Methods:** We aimed to characterize and compare Rome IV and Rome III FD prevalence in the general adult population across multiple countries by using data from a large three-country internet survey conducted on behalf of the Rome Foundation. The survey included the Rome IV Diagnostic Questionnaire for Adults, the Rome III diagnostic questions for FD, and demographic and health history questions, and was completed in 2015 by a community sample of individuals aged 18+ in the US, UK and Canada (2,100 in each country). Quota-based sampling ensured equal proportion of sex (50%/50%) and age groups (40% aged 18–39, 40% aged 40–64, 20% aged 65+) across countries, and controlled education distributions (30% maximum with college degree or equivalent). Latest national census figures were used to calculate correction weights for age (in 5-year bins) and gender proportions and obtain census-adjusted FD prevalence estimates for each country.
**Results:** Of 6,300 total response sets, 5,931 were judged valid for analysis (49.2% female; mean age = 47.4 years, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after data from inconsistent responders were eliminated. Sex and age group proportions were equivalent between countries since the sampling was quota-based. Raw and census-weighted (in parentheses) FD prevalence by Rome IV vs. Rome III criteria was 11.9% (12.7%) vs. 9.4% (10.0%) in the US, 8.4% (8.7%) vs. 7.2% (7.3%) in Canada, and 7.6% (7.7%) vs. 5.9% (6.0%) in the UK. FD prevalence was significantly higher for Rome IV vs. Rome III criteria in the total sample (raw sample prevalence 9.3% vs. 7.5%, $p < 0.0001$). The US sample had higher ($p < 0.05$) Rome III FD rate than the other countries, and a higher Rome IV rate than the UK. In the total sample, women had substantially higher FD rates than men (Rome IV: 11.3% vs. 7.3%; $p < 0.0001$. Rome III: 9.9% vs. 5.1%; $p < 0.0001$), and individuals aged 65+ had lower FD rates than younger ones (Rome IV: 5.4% vs. 10.3%; $p < 0.0001$. Rome III: 4.8 vs. 8.2; $p < 0.0001$). The distribution of IBS prevalence across age and sex groups is presented in the Table. Among individuals who met Rome IV FD criteria, 61.5% classified as having Postprandial Distress Syndrome (PDS), 17.6% as EPS and 20.9% as both. With Rome III criteria, 77% of FD cases classified as PDS, only 0.5% as EPS (due to the multiple symptom exclusions required by Rome III), and 22.5% as neither.

**Table:** Population Rome III and Rome IV FD rates (%) by sex and age groups in the US, UK and Canada survey samples (without census weighting).

| Rome III FD: | Age 18–34 | Age 35–49 | Age 50–64 | 65+ | All age groups |
|---|---|---|---|---|---|
| US Females (n = 962) | 14.5% | 14.9% | 12.6% | 8.9% | 12.9% |
| US Males (n = 987) | 6.9% | 7.8% | 5.0% | 4.7% | 6.1% |
| UK Females (n = 976) | 9.4% | 7.5% | 7.3% | 2.5% | 7.3% |
| UK Males (n = 1018) | 2.2% | 6.0% | 6.5% | 2.8% | 4.5% |
| Canada Females (n = 980) | 7.9% | 8.6% | 13.7% | 7.1% | 9.6% |
| Canada Males (n = 1008) | 5.3% | 6.4% | 4.3% | 3.8% | 4.9% |
| Total Sample (N = 5,931) | 7.8% | 8.6% | 8.3% | 4.8% | 7.5% |
| **Rome IV FD:** | **Age 18–34** | **Age 35–49** | **Age 50–64** | **Age 65+** | **All age groups** |
| US Females (n = 962) | 17.2% | 17.4% | 13.4 | 8.3% | 14.4% |
| US Males (n = 987) | 13.8% | 8.3% | 8.8% | 5.1% | 9.5% |
| UK Females (n = 976) | 13.6% | 7.9% | 9.5% | 2.5% | 9.3% |
| UK Males (n = 1018) | 5.8% | 6.4% | 8.5% | 2.8% | 6.0% |
| Canada Females (n = 980) | 10.7% | 10.2% | 11.6% | 8.2% | 10.4% |
| Canada Males (n = 1008) | 8.5% | 6.9% | 4.6% | 5.9% | 6.5% |
| Total Sample (N = 5,931) | 11.8% | 9.6% | 9.4% | 5.4% | 9.3% |

**Conclusion:** In the three nations sampled, 7.7% to 12.7% of the adult population meets Rome IV FD criteria and 6.0% to 10.0% meets Rome III FD criteria. FD is more prevalent in the US than in Canada or the UK, and is female-predominant and less common in older adults (age 65+). EPS emerges as a more prevalent FD subtype in Rome IV compared to Rome III due to easing of diagnostic restrictions. [Supported by the Rome Foundation]
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## P0971 LOW YIELD REPEAT UPPER GI ENDOSCOPY FOR DYSPEPSIA PATIENTS: CONSECUTIVE SERIE FROM A TERTIARY REFERRAL CENTER

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**Introduction:** In patients with persistent dyspeptic symptoms, the benefit of repeating upper gastrointestinal endoscopy is unclear.
**Aims & Methods: Objectives of the study:** To evaluate endoscopic and histological findings in patients who undergo endoscopy for dyspeptic symptoms; evaluate how frequently endoscopy was repeated and whether there were changes in endoscopic/histologic findings in patients with persistent dyspeptic symptoms. **Methods:** Retrospective cohort study of all patients with dyspepsia scheduled for upper gastrointestinal endoscopy (UGE) between January 2010 and December 2012; Endoscopic follow-up until December 2015. Exclusion criteria: Prior gastric surgery or alarm symptoms highly suggestive of neoplasia. We defined organic cause for dyspepsia as peptic ulcer disease (PUD), gastroesophageal reflux disease or malignancy. Some patients had more than one positive endoscopy findings.
**Results:** The study sample included 2150 patients with average age of $54 \pm 16$ years of whom 62% were female. The average follow-up was $4.6 \pm 0.9$ years. Endoscopic/histologic findings at baseline endoscopy: normal or insignificant findings in 69.3% (1491), erosive gastroduodenitis in 14.4%, esophagitis in 7.1%, gastric polyp in 4.4%, PUD in 3.4%, Barret's esophagus in 1.2%, portal hypertension in 0.6%, malignancy in 0.7% and dysplasia in 0.3%. Patients aged $\geq$ 50 years had a trend for higher prevalence of organic cause of dyspepsia compared to those aged $<$50 years (66.0% vs 34.0%; OR 1.27; 95% CI:0.96–1.68, $p = 0.056$). Just 1/16 patients (6.2%) with malignancy at baseline endoscopy was $<$50 years old. Biopsies at baseline endoscopy were taken in 70% (1504) of patients: *H. pylori* infection in 41% (615), non-atrophic gastritis in 80% (1206) and atrophic gastritis in 19% (281). A subsequent endoscopy was performed in 83 patients for reasons other than dyspepsia, and these patients were not considered in the further analysis. UGE was repeated in 21.9% (452/2067 patients). The median time to subsequent endoscopy was 24 months (range 2–70) years and median number of UGEs/patient was 2 (range 1–10). The endoscopic/histologic findings in patients with subsequent UGE for persistent dyspepsia were: normal or insignificant findings in 78.6%, erosive gastroduodenitis in 11.9%, gastric polyp in 7.7% esophagitis in 3.3%, PUD in 2.4%, malignancy in 0.2% and dysplasia in 0.2%. The diagnostic yield of endoscopy in detecting organic causes for dyspepsia was higher for the initial UGE (11.3%) than the subsequent UGE (OR = 2.6; 95% CI: 0.92–7.5, $p = 0.07$), even when considering only patients aged $\geq$50 years (52.4% vs. 47.6%).
**Conclusion:** The diagnostic yield of UGE in patients with dyspepsia without alarm symptoms for organic causes was low with almost 2/3 of patients having a normal baseline endoscopy. However, there is a trend for a higher diagnostic yield for organic causes for dyspepsia in patients aged $\geq$50 years. Repeating endoscopies in patients with persistent dyspepsia does not seem to be clinically justified.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0972 EVIDENCE FOR ANTIOXIDATIVE AND ANTIINFLAMMATORY PROPERTIES OF CARBON MONOXIDE AND HYDROGEN SULFIDE IN PATHOPHYSIOLOGY OF ASPIRIN-INDUCED GASTRIC DAMAGE

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**Introduction:** Carbon monoxide (CO), hydrogen sulfide ($H_2S$) and nitric oxide (NO) are endogenous mediators. CO is produced via activity of constitutive heme oxygenase (HO)-2 and inducible by inflammation and oxidative stress HO-1. $H_2S$ is produced endogenously by cystationine-$\gamma$-lyase (CSE), cystationine-$\beta$-synthase (CBS) and 3-mercaptopyruvate sulfurtransferase (3-MST). Both, CO and $H_2S$ were shown to protect gastric mucosa against injury induced by topical irritants, such as ethanol or stress. We investigated if CO and $H_2S$ exert gastroprotection against aspirin (ASA)-induced gastric damage in animal model and whether increased bioavailability of CO or $H_2S$ can affect this injury via regulation of gastric microcirculation, lipid peroxidation and expression of antioxidative enzymes in gastric mucosa. Moreover, we investigated involvement of NO in the mechanism of CO-mediated gastroprotection.
**Aims & Methods:** Male Wistar rats were pretreated with A) vehicle, B) CORM-2 (5 mg/kg i.g.) alone or in combination with NO synthase (NOS) inhibitor, L-NNA (10 mg/kg i.p.), C) ZnPP (10 mg/kg i.p.), an inhibitor of HO-1 or D) NaHS (5 mg/kg i.g.), $H_2S$ donor, E) D,L-propargylglycine (PAG, 30 mg/kg i.g.), an inhibitor of CSE. Next, ASA in the dose of 125 mg/kg was administered i.g. to induce gastric damage. The area of ASA-induced gastric mucosal damage was evaluated macroscopically by planimetry. Gastric blood flow (GBF) was measured by laser Doppler flowmeter. CO content in gastric mucosa and COHb level in blood samples were determined by gas chromatography. Protein and mRNA expression for Nrf-2, HO-1, HO-2, CSE, CBS, 3-MST, inducible NOS (iNOS), glutathione peroxidase (GPx)-1, superoxide dysmutase (SOD)-1 were measured by Western Blot and/or real-time PCR. Malonylodialdehyde (MDA) level was measured using spectrophotometric assay.
**Results:** In gastric mucosa with aspirin-induced damage, HO-1 and iNOS mRNA and protein expressions were increased in paralel to Nrf-2, while HO-2, CSE and 3-MST expression was downregulated. CORM-2 and NaHS but not ZnPP or PAG decreased ASA-induced gastric damage, and this effect was accompanied by the increase of GBF. CORM-2 significantly enhanced mRNA and protein expression for Nrf-2, HO-1, CSE, CBS, GPx-1, SOD-1 and increased CO content in gastric mucosa and COHb level in blood. However, NaHS decreased mRNA and protein expression for iNOS, HO-1 and Nrf-2, increased expression for GPx-1 and SOD-1 but did not affect expression for CSE, CBS, 3-MST and CO content in gastric mucosa. MDA level was decreased after NaHS or CORM-2 administration as compared with vehicle-control group. Interestingly, L-NNA did not affect protective effect of CORM-2 and CO-induced reduction of lipid peroxidation.
**Conclusion:** We conclude that CO and $H_2S$ are important components of protective and physiological gastric mucosal barrier. Increased bioavailability of CO produced by HO-1/Nrf-2 pathway or released from CORM-2 and increased $H_2S$ content after NaHS or enhanced biosynthesis prevent gastric mucosa against ASA-inudced gastric damage via upregulation of gastric microcirculation, downregulation of lipid peroxidation and antiinflammatory properties of these gaseous molecules. This study was supported by a grant from National Science Centre in Poland (UMO-2014/15/N/NZ4/04564).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0973 USE OF DISTENSIBILITY TESTING TO DEMOSTRATE PYLORIC FUNCTION IN A PORCINE MODEL

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**Introduction:** Pyloric sphincter function is still relatively poorly understood. Its role in digestive function and in disease require investigation and enquiry in order to understand its function. The functional lumen imaging probe (FLIP) is a relatively new technique which uses a distensible cylindrical balloon to characterise valvular regions in the digestive tract. However to date there are very few studies to determine if FLIP can be useful in measuring pyloric sphincter function.
**Aims & Methods:** The aim of this study was to identify if new information on the function of the pylorus could be identified by inflating a FLIP probe in the pylorus using a distensibility protocol. With local ethics approval two anaesthetised pigs were used for this study (28 kg). With the pigs in the supine position the gastroscope was advanced into the stomach with a clear view of the pylorus. The EndoFLIP(R) catheter was then inserted into the biopsy channel and pushed out of the distal end of the endoscope. The probe was then placed straddling the pyloric sphincter and its position was confirmed by filling 20 ml of liquid into the balloon and observing the classic hourglass shape on the system screen. The balloon was then deflated and the pressure was set to 0 mmHg in order to establish a baseline. A stepwise inflation protocol was then carried out to 20 ml, 30 ml, 40 ml and 50 ml. Each step was held for at least 20 sec. The protocol was repeated. Then a ramp distension from 0 to 50 ml was carried out and immediate deflation at the same rate. After 1.5 ml of neostigmine was injected intraveniously and a wait of 5 minutes the stepwise and ramp protocols were repeated. After 30 mins a test distension identified that the effects of the neostigmine were no longer apparent and a further set of stepwise and ramp distensions carried out. Then using a feeding tube a mixture of 300 ml of baby formula and 150 ml of water was infused into the stomach and the stepwise protocol was repeated immediately after and again after a 30 min interval.
**Results:** Table 1 shows the results for densibility index (minimum CSA/pressure) at 30 ml, 40 ml and 50 ml volumes for the two pigs studied. The higher value the higher distensibility.

**Table 1.**

| Pig1 | Baseline | Post Neostigmine | 1 hr Post Neostigmine | Immediate Post Food | 30mins Post Food |
|---|---|---|---|---|---|
| 30 ml | 17 | 18 | 10.8 | 45.4 | 19.1 |
| 40 ml | 13.8 | 12 | 11.3 | 40.5 | 17.5 |
| 50 ml | 7 | 8.3 | 8.3 | 9.3 | 10.5 |
| Pig 2 | | | | | |
| 30 ml | 19 | 5.4 | 9.6 | 33.3 | 15.9 |
| 40 ml | 9.1 | 6.4 | 8.3 | 21.4 | 9.5 |
| 50 ml | 6.6 | 5.5 | 7.3 | 10.3 | 6.7 |

**Conclusion:** These results show that using EndoFLIP we can clearly see how the pyloric sphincter behaves like a valve, Using Neostigmine we were able to provoke a decrease in the distensibility of the pylorus in the two pigs. By placing food in the stomach during the test we have been able to show that in both pigs the pylorus became more distensible (more relaxed) as indicated by the increase in the distensibility index. This technique shows promise as a method to determine pyloric function in health and disease. However further studies are needed to verify this.
**Disclosure of Interest:** B.P. McMahon: Barry McMahon is a minor shareholder with Crospon Ltd Ireland.
All other authors have declared no conflicts of interest.

## P0974 ACCELERATION OF EXPERIMENTAL GASTRIC ULCER HEALING BY MELATONIN. EVIDENCE FOR THE INTERACTION OF MELATONIN WITH MEL RECEPTORS AND MUCOSAL REGENERATING FACTORS EGF AND IGF-1 AND THEIR RECEPTORS

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**Introduction:** Melatonin is a pineal gland hormone with a potent reactive oxygen metabolite scavenging and antioxidant activities also produced in abundant amounts by gastrointestinal mucosa. This indoleamine plays an important role in protection against noxious agents and the mechanism of gastric ulcer healing. However, the expression of G-protein coupled melatonin receptors Mel1 and Mel2 in normal and/or ulcerated gastric mucosa and their relationship with trophic physiological factors including epidermal growth factor (EGF), insulin like growth factor-1 (IGF-1), and their receptors (IGF-1 R and EGF-R) during the course of gastric ulcer healing have been little studied.
**Aims & Methods:** To determine the effect of treatment with melatonin and expression of Mel1 and Mel2 receptors, growth factors EGF and IGF and their receptors during ulcer healing, GU were produced in rats by a focal, serosal application of 100% acetic acid. Rats with GU were treated 9 days with vehicle (saline) and melatonin (20 mg/kg-d i.g.) Rats were euthanized at different time intervals post-GU induction and the gastric blood flow was examined at ulcer margin and non-ulcerated gastric mucosa, the area of GU was measured by planimetry and the mucosal specimens were collected for the quantitative histology and the Mel1-, Mel2 receptors, EGF-R, IGF-1 and IGF-1 R and signal quantification were assessed using Metamorph 7 image system.
**Results:** Melatonin significantly decreased the size of GU and increased the GBF at ulcer margin at day 9$^{th}$ upon ulcer induction compared with vehicle ($p < 0.05$). In non-ulcerated stomach, Mel1 and Mel2 were expressed in: a) neuronal and glial cells of submucosal and myenteric plexuses, b) endothelial cells of blood vessels and c) in epithelial progenitor cells and surface epithelium. Signal intensity was highest in the neuronal cells ($100 \pm 4$ IU) followed by endothelial cells ($56 \pm 3$ IU; $p < 0.01$) and epithelial cells ($44 \pm 3$ IU; $p < 0.01$). Expression of Mel1 in epithelial cells was 2.1 fold stronger than Mel2 ($p < 0.01$). In the scars of healed GU neuronal cells in submucosal plexus were significantly reduced ($p < 0.001$) and Mel1 and Mel2 were reduced and/or absent. Regenerated mucosa of GU scar was lined with dilated, irregular glands, which either expressed both Mel1 and Mel2 (1.8-fold less than Mel1;

$p < 0.01$) or were Mel1 and Mel2 deficient (~24% of glands). Expression of EGF-R, IGF-1 and IGF-1 R in regenerated epithelium of GU scar was mostly co-localized with Mel1. Quantitatively expression of EGF-R was > than IGF-1 R and > IGF-1.

**Conclusion:** 1) In normal stomach, melatonin receptors Mel1 and Mel2 are expressed in neuronal cells of submucosal and myenteric plexuses, endothelial cells of blood vessels, and in epithelial progenitor cells and surface epithelium; 2) melatonin accelerates ulcer healing via an increase in gastric microcirculation around the ulcer; 3) in scars of healed GU expression Mel1 and Mel2 is significantly reduced in neuronal cells and this is improved by treatment with melatonin; 3) expression of Mel1 and Mel2 is increased ($p < 0.01$) in regenerated epithelium, where it co-localizes to EGF-R, IGF-1 and IGF-1 R, indicating their local interactions during GU healing; 3) a lack of Mel1 and Mel2 in some regenerating glands may indicate an existence of 2 distinct cell lineages, and 4) differential distribution of Mel1 and Mel2 receptors in gastric mucosa indicates targets for melatonin hormonal (e.g. endothelial cells) as well as paracrine and autocrine actions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0975 A NEW GASTRIC ACID SUPPRESSOR, "VONOPRAZAN", IS EFFECTIVE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE REFRACTORY TO PROTON PUMP INHIBITORS

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**Introduction:** Acid suppression is the mainstay of therapy for gastro-esophageal reflux disease (GERD), and proton pump inhibitors (PPIs) are the first choice of treatment. However, approximately 30% of patients with GERD experience persistent symptoms while taking PPIs. Previous reports have showed that the acid suppression ability of PPIs is affected by the following: (1) there is a large variation in efficacy among patients because of the cytochrome P450 (CYP) 2C19 genotype; (2) PPIs are unable to continuously control acid secretions for a period of 24 h; and (3) acid suppression is lower in patients without *Helicobacter pylori* infection than in those with the infection. Taking these finding into consideration, PPIs may be insufficient for controlling reflux symptoms in patients with GERD. Vonoprazan (VPZ) belongs to a new class of gastric acid-suppressing agents developed in Japan. It has potent and long-lasting anti-secretory effects resulting in a greater acid suppression than conventional PPIs (1).

**Aims & Methods:** The aim of this study was to investigate the effect of switching from PPIs to VPZ in patients with GERD, who have persistent symptoms despite treatment with PPIs. Sixteen patients with GERD, who have persistent reflux symptoms (heartburn and/or regurgitation at least once a week) despite treatment with PPIs were enrolled in this study. All patients were endoscopically diagnosed with non-erosive reflux disease. Patients received VPZ 20 mg daily for 4 weeks, and were assessed for the severity of heartburn (score 0–3), regurgitation (score 0–3), and summation of the heartburn and regurgitation scores (reflux symptoms score, range 0–6) before, and after 2 weeks and 4 weeks of VPZ administration. The primary endpoint was the therapeutic effect of switching from PPIs to VPZ. Complete resolution was considered when the reflux symptoms score was zero. Data were described as mean (SD). Categorized data were analyzed by $\chi 2$ test or Fisher's exact. Changes in symptom scores were analyzed using one-way analysis of variance (ANOVA). A P value of $<0.05$ was considered as significant.

**Results:** The heartburn scores at baseline, and at 2 and 4 weeks after treatment were 1.81 (1.83), 1.25 (1.12), and 1.0 (0.81) respectively. There was a significant difference between the scores at baseline and after 4 weeks ($p = 0.049$). Regurgitation scores at baseline, and at 2 and 4 weeks after treatment were 1.62 (0.88), 1.25 (1.06), and 1.06 (0.85) respectively; the scores were not significantly different from each other ($p = 0.236$). Reflux symptoms scores were 3.43 (1.26) at baseline, 2.50 (1.96) at 2 weeks, and 2.06 (1.61) at 4 weeks. A tendency for reduction in the reflux symptoms score was found at 2 weeks and at 4 weeks; however, it was of no statistical significance ($p = 0.063$). Four patients (25.0%) had complete resolution by week 2 while five patients (31.2%) had complete resolution by week 4.

**Conclusion:** The results of this study indicate that switching from PPIs to VPZ may be an effective therapy for patients with PPI-refractory reflux symptoms.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0976 THE OVERLAP BETWEEN IRRITABLE BOWEL SYNDROME AND FUNCTIONAL DYSPEPSIA IN KOREA: ASSOCIATION OF SLC6A4 5-HTTLPR AND TRPV1 945 G > C

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**Introduction:** Irritable bowel syndrome (IBS) and functional dyspepsia (FD) show considerable overlap.

**Aims & Methods:** The present study aimed to investigate the clinicodemographic features of FD, IBS and FD-IBS overlap. It also evaluated the potential risk factors for FD-IBS overlap including genetic polymorphism such as SLC6A4 5-HTTLPR, ADRA2A 1291C > G, GNB3 825C > T, CCK1R intron 779 T > C and TRPV1 945 G > C. Study subjects were prospectively recruited at Gastroenterologic clinic of Seoul National University Bundang Hospital between 2003 and 2014. Three hundred and fifty four FD patients and 278 controls were enrolled.

**Results:** The prevalence of IBS in FD was 35.7% (110/308) and that of FD in IBS was 70.5% (110/156). Patients with the FD-IBS overlap showed severer degree of bloating, nausea and general abdominal discomfort than either FD or IBS-alone patients (all $P < 0.05$). In multivariable analyses, nausea, postprandial fullness, SLC6A4 5-HTTLPR L/L and ADRA2A-1291 G/G were risk factor for the FD-IBS overlap among the patients with FD ($P < 0.05$). Among patients with IBS, increasing age, single/unmarried status, nausea, bloating and feeling of incomplete emptying were significantly associated with an increased risk of the overlap. Among patients with both FD and IBS, IBS-C was more common in PDS group than EPS (55% and 0%, $P = 0.035$).

**Conclusion:** The prevalence of FD-IBS overlap was considerably high and its symptom severity was severer compared to the single disorder. SLC6A4 5-HTTLPR and ADRA2A- 1291 polymorphism might be risk factors for the overlap in patients with FD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0977 THE PREDICTIVE VALUE OF A DISTINCT LABORATORY SCORE IN THE PREDICTION OF DELAYED GASTRIC EMPTYING AND AUTONOMIC NERVE DYSFUNCTION IN PATIENTS WITH AUTOIMMUNE GASTRITIS

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**Introduction:** Symptoms of patients with autoimmune gastritis are proteiform and some patients may present with symptoms suggestive of delayed gastric emptying (GE). Signs of autonomic nervous system dysfunction exist in patients with autoimmune diseases. Some of the patients with autoimmune gastritis may have delayed GE causing upper gastrointestinal (GI) symptoms and this situation may be related to autonomic nerve dysfunction.

**Aims & Methods:** The aims of this study were to investigate the predictive value of two scoring systems in the differentiation of delayed gastric emptying and deranged autonomic nerve function in patients with autoimmune gastritis. 154 patients (106 women) diagnosed as having autoimmune gastritis and 65 functional dyspepsia patients whose gastric emptying test were available, were analyzed by using two laboratory based scoring systems: "global score" (hemoglobin, mean corpuscular volume, gastrin, vitamin $B_{12}$ and chromogranin A) and "simple score" (hemoglobin, mean corpuscular volume, gastrin).

**Results:** The mean "simple score" was $4.82 \pm 0.94$ for autoimmune gastritis patients with delayed gastric emptying and $0.72 \pm 0.60$ for patients with normal gastric emptying ($p < 0.001$, AUC: 97.2, PPV: 97.6% and NPV: 100%). The mean "global score" was $7.42 \pm 0.81$ for AIG patients with delayed gastric emptying and $1.176 \pm 0.98$ ($p < 0.001$) for patients with normal gastric emptying (AUC: 98.8, positive predictive value: 99.1% and negative predictive value: 82.6%). Mean simple score was significantly lower in patients with normal autonomic nerve function compared to patients with deranged autonomic nerve function ($0.908 \pm 0.409$ vs $3.55 \pm 1.88$ $p < 0.001$, AUC: 88.3, PPV: 97.5% and NPV: 66.6%, 95% CI 88.4–99.7).

**Conclusion:** Our results showed that this model may help physicians while evaluating AIG patients and deciding which patients need gastric emptying test. Therefore, we suggest that gastric emptying study should be ordered in patients who are fulfilling the criteria proposed by these scoring systems.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0978 EFFECTS OF PROTON PUMP INHIBITORS AND GENDER DIFFERENCE ON SERUM GASTRIN LEVELS

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**Introduction:** Gastrin is an acid secretion-stimulating hormone, which is affected by several factors including pH in the stomach, mucosal injury and gender[1), 2)]. Proton pump inhibitors (PPIs) are commonly adopted for disorders caused by hyperacidity, and the use of PPIs is known to lead hypergastrinemia[3)]. Although H.pylori infection is known to induce hypergastrinemia[4)], the data of the gastrin levels in the patients with atrophic gastritis taking long-term PPIs is still lacking.

**Aims & Methods:** To investigate the factors elevating serum gastrin levels, we conducted this study. H. pylori status was determined by the presence of serum H. pylori IgG and serum gastrin levels were measured by RIA. Atrophic gastritis was assessed by upper gastrointestinal endoscopies performed by experienced endoscopists.

**Results:**

| Conparison items | | p |
|---|---|---|
| Use of PPIs | | |
| Non-drug users (n = 91) | PPI users (n = 175) | |
| 88.4 (66.9–166.2) | 219.1 (143.5–425.4) | < 0.001 |
| Gender | | |
| Men (n = 61) | Women (n = 205) | |
| 151.7 (86.3–286.3) | 226.1 (121.6–466.7) | 0.001 |
| H.pylori infection | | |
| Controls (n = 143) | Infected (n = 123) | |
| 153.3 (80.6–333.2) | 185.2 (109.5–336.9) | 0.064 |

323 patients (84 men and 239 women) were enrolled. Median serum gastrin levels were higher in PPI users than non-antacid users (219.1 vs. 88.4 $p < 0.001$) and in women than men (226.1 vs. 151.7 $p = 0.001$). The gender difference was confirmed in the subgroup taking PPIs ($p = 0.001$), but not among the non-users. There was no significant difference in gastrin levels among three kinds of PPIs (lansoprazole, rabeprazole, and esomeprazole). Multivariate analysis revealed that gastrin levels over 150 pg/ml were significantly associated with PPI use (OR = 7.23 CI 4.02–13.01) and women (OR = 2.32 CI 1.16–4.62). H.pylori infection and atrophic gastritis were not associated with hypergastrinemia.

**Conclusion:** Each PPI was associated with hypergastrinemia equivalently and the serum gastrin levels in PPI users were higher than $H_2$ antagonist users. Serum gastrin levels in women were higher than men, and the differences were greater especially in PPI users.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0979 THE EFFECT OF K027, A NOVEL OXIME ACETYLCHOLINESTERASE REACTIVATOR, ON OESOPHAGEAL MOTOR FUNCTION IN EXPERIMENTAL PIGS

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**Introduction:** Reactivators of acetylcholinesterase (AChE) are essential in the treatment of organophosphate intoxication. Wider clinical use of several AChE modulators is limited because of the significant side effects, including serious gastrointestinal toxicity. Our research team has synthesised our own priority compound K027, 1-(4-carbamoylpyridinium)-3-(4-hydroxyiminomethylpyridinium)-propane dibromide. This novel oxime AChE reactivator was already tested in vitro and on small laboratory animals with excellent results. K027 might thus be a candidate for human therapeutic use in the event of industrial poisoning or catastrophic situations. The small adult pig can be used in experiments as an omnivorous representative due to its relatively very similar gastrointestinal functions in comparison to man. The aim of this study was to evaluate the effect of K027 on porcine oesophageal manometry.

**Aims & Methods:** Ten mature experimental pigs entered the study (Sus scrofa f. domestica, 3–4-month old; 5 males, 5 females; mean weight $32.0 \pm 4.6$ kg). All recordings were performed under general anaesthesia in the morning after 24 hours of fasting. Water-perfused disposable catheters were used (MMS G-88402, conventional 12 French, 8 channels with central lumen; MMS – Medical Measurement Systems B.V., Enschede, the Netherlands). Catheters were introduced into the oesophagus through mouth, their correct position was verified endoscopically. Basic oesophageal manometry was performed for 10 minutes by means of the Polygraf UPS 2020 (UPS-2020 manometry system from MMS – Medical Measurement Systems B.V., Enschede, the Netherlands). After this baseline period, K027 (1500 mg i.m.) was administered. Trial manometry started 19 minutes later (at the $t_{max}$ point, with $C_{max}$ 106 $\mu$g/mL). Dry swallowing was induced by massage of lower part of the neck. All evaluated parameters were assessed as an average measure of four consecutive values.

**Results:** Male and female pigs were comparable in age and weight. In female pigs, there were higher baseline pressures of the lower esophageal sphincter ($19.2 \pm 13.0$ vs. $13.0 \pm 1.6$ mm Hg; NS) and peristaltic wave pressures ($34.2 \pm 11.5$ vs. $21.6 \pm 3.4$ mm Hg; $p = 0.046$). Mean relaxation of the lower esophageal sphincter was $96.7 \pm 5.4\%$, duration of relaxation was $6.7 \pm 6.1$ seconds. Mean duration of peristaltic wave was $2.3 \pm 1.0$ seconds. These two time intervals were longer in female pigs, however, the difference did not reach a statistical significance. K027 did not produce any significant changes of the principal manometry indices (1 – type 2 error beta < 0.8).

**Conclusion:** Oesophageal manometry in experimental pigs is feasible. Porcine resting and relaxed pressures of the lower esophageal sphincter are fully comparable with healthy human subjects. Evocable swallowing is doable and oesophageal peristalsis is quantifiable. K027, a novel AChE reactivator, caused only non-significant minor changes of the major parameters of porcine oesophageal manometry.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0980 BRAIN MECHANISMS UNDERLYING THE EFFECT OF MOTILIN RECEPTOR AGONIST ERYTHROMYCIN ON HUNGER FEELINGS IN HEALTHY VOLUNTEERS

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**Introduction:** We have previously shown that infusion of 40 mg of the motilin receptor agonist, erythromycin (EM), induces peaks in fasting hunger ratings, accompanied by a premature gastric phase III of the migrating motor complex (MMC). It is likely that the sensation of hunger during motilin receptor stimulation results from changes in brain activity in regions involved in the regulation of appetite and food intake.

**Aims & Methods:** Aim of the study: To explore the neural and hormonal responses to intravenous EM infusion and its influence on eating behavior measurements and hedonic food intake in healthy volunteers. Methods: Thirteen healthy right-handed women were recruited for this counterbalanced 2-visit study. On each study day, subjects were given a 275 kcal standard breakfast after an overnight fast. Hundred-and-five minutes after breakfast, intravenous cannulas were inserted into a vein on both forearms; 10 minutes later subjects entered the magnetic resonance (MR) scanner for a 10 minutes adaptation period after which MR images were acquired for 50 minutes. Ten minutes after the start of scanning, 40 mg EM or saline were intravenously infused over 20 minutes. Blood was taken from the other cannula before and every 10 minutes after the start of the infusion until the end point of the study to measure plasma motilin levels. Hunger ratings (visual analogue scale) were obtained every 5 minutes during scanning. After scanning, subjects drank chocolate milkshake ad libitum as a measure of hedonic eating. Preprocessing and analysis were performed in SPM12. The effect of EM versus saline infusion on brain responses in a priori defined regions of interest (ROI) was assessed using one-way ANOVA, with time (1 min bins) as within-subject factor, at a voxel-level threshold of pFWE-corrected < 0.05 combined with an extent threshold of kE > 10. The ROIs consisted of brain regions involved in homeostatic and hedonic control of feeding. Percentage change of the plasma motilin levels (compared to baseline) was calculated using the mixed model procedure from SAS 9.2.

**Results:** EM infusion deactivated left anterior cingulate cortex, left thalamus, and right insula. In contrast, activation of left caudate, left orbital frontal cortex, left putamen, left amygdala, midbrain, and accumbens were observed during EM infusion. The effects started 10–15 minutes and reached a peak 35 minutes after the start of infusion. Plasma motilin levels increased significantly higher after saline infusion than after EM infusion ($p < 0.0001$, mixed model). In addition, hunger ratings (increase from baseline) and milkshake intake ($p < 0.0001$, and $p = 0.044$, respectively, paired Student's t- test, one-tailed) were significantly higher after EM compared to saline. Furthermore the peak in hunger ratings coincided with the peak in the brain responses.
**Conclusion:** Intravenous infusion of the motilin agonist EM affects hunger ratings, hedonic food intake and activity in brain regions related to homeostatic and hedonic control of appetite and feeding. The effect seems not to be mediated via stimulation of motilin release.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0981 SOMATIZATION IS THE KEY LINK IN THE OVERLAP BETWEEN FUNCTIONAL GASTROINTESTINAL DISORDERS AND OTHER FUNCTIONAL SOMATIC SYNDROMES

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**Introduction:** Functional gastrointestinal disorders are often associated with pain and result in reduced quality-of-life for individuals affected. They are also associated with elevated anxiety[1] and a tendency to somatization [2] in which psychological distress receives apparent somatic expression. Similar findings have been reported in other functional somatic syndromes such as chronic pain and fibromyalgia. The extent to which these associations are specific to gastrointestinal disorders has not been studied.
**Aims & Methods:** This study aimed to 1) estimate the overlap between functional gastrointestinal (GI) and extra-GI conditions within individuals, 2) compare level of GI and extra-GI symptom burden in sufferers of GI and extra-GI disorders and 3) compare the correlation between somatization and symptom burden in sufferers of GI and extra-GI disorders. A similar pattern of correlation in GI and extra-GI groups would suggest a common role for somatization in symptom burden for both GI and extra-GI functional conditions. Individuals were sampled from gastroenterology clinics, chiropractic clinics and community samples screened for GI symptoms occurring more than rarely. Standard diagnostic criteria for applied to GI disorders (Rome III) and extra-GI conditions (chronic pain, lower back pain, fibromyalgia, chronic fatigue). All individuals completed standardized measures of GI and extra-GI symptom burden, including the gastrointestinal symptom rating scale (GSRS). Due to overlap, individuals were categorized as meeting criteria for FGID only, extra-GI only, both FGID and extra GI or neither. The final group did not meet criteria but did experience GI or extra GI symptoms and are considered subsyndromal.
**Results:** A total of 133 individuals were recruited and grouped as per Table 1. 23% did not meet formal criteria for either gastrointestinal or extra-GI syndromes so are considered subsyndromal. Among individuals who qualified for FGID or extra-GI syndromes 39% met criteria for both. Mean GSRS scores were higher in groups meeting FGID criteria but only by degree. Somatic pain intensity scores were highest in groups meeting extra-GI criteria but also elevated in FGIDs (Table 1).

**Table 1:** Overlap, burden and psychological associations. Table entries are a) mean (SD) or b) Pearson correlation coefficient

| Measure | Sub-syndromal (n = 31) | FGID (n = 20) | Extra-GI (n = 40) | Both (n = 38) |
|---|---|---|---|---|
| GSRS[a] | 28.8 (9.8) | 42.0 (14.4) | 31.1 (11.7) | 41.9 (14.1) |
| Somatic pain[a] | 29.9 (20.4) | 40.5 (21.8) | 32.4 (18.4) | 43.6 (21.0) |
| Anxiety[a] | 12.5 (4.0) | 12.3 (3.5) | 11.6 (3.9) | 12.0 (4.6) |
| Somatisation[a] | 24.5 (5.1) | 27.2 (3.7) | 24.9 (4.6) | 27.6 (4.9) |
| $r_{GSRS/somatization}$[b] | 0.45 | 0.52 | 0.55 | 0.45 |
| $r_{Pain/somatization}$[b] | 0.63 | 0.41 | 0.38 | 0.21 |

The correlation between somatization and both gastrointestinal symptoms burden (GSRS) and extra-GI somatic pain intensity was moderate to strong in all groups including those who did not meet criteria but were subsyndromal (Table 1).
**Conclusion:** There is substantial overlap between GI and extra-GI somatic disorders. Although somatization levels are elevated in FGIDs compared with extra-GI syndromes the correlation between somatization and both somatic pain and GSRS is relatively similar across conditions. This suggests that somatization may be a common factor in the brain-gut connection across FGID and extra-GI functional somatic syndromes.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0982 AN INCREASED PREVALENCE OF NEURODEGENERATIVE/ DEMYELINATING PROCESSES IN PATIENTS WITH ESOPHAGEAL ACHALASIA – A PROSPECTIVE STUDY

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**Introduction:** There are no studies examining a possible relationship between achalasia and neurodegenerative/ demyelinating diseases of central nervous system. Although both achalasia and neurodegenerative/demyelinating processes are not considered hereditary, a number of genetic variations have been shown to increase the risk of both conditions. For example, HLA-DQB1-insertion (chromosome 6) may be strongly associated with both achalasia and multiple sclerosis suggesting that autoimmune processes are involved in their etiopathogenesis. Several other findings (e.g. inflammatory infiltrate, Lewýs bodies, north-south gradient etc.) are also described in patients with achalasia as well as with neurodegenerative/demyelinating diseases.
**Aims & Methods:** The aim of our prospective study was to examine a prevalence of neurodegenerative/demyelinating diseases in a cohort of consecutive patients with confirmed esophageal achalasia. Achalasia was diagnosed by high resolution manometry, endoscopy and X-ray. One hundred and forty consecutive patients with achalasia (female/male, mean age) have been questioned so far by using a detailed questionnaire about the occurrence of neurological symptoms or diseases in their personal or family history. Those with suspicion of a neurological disease were referred for MR imaging of the brain and for detailed neurological examination.
**Results:** A total of 51 out of 140 patients (35.4%) described a presence of neurological symptoms – most often visual disturbances in 33.3% (17 pts.), paresthesia of limbs in 23.5% (12 pts.) and hypotension in 19.6% (10 pts.). A total of 6 patients (4.3%) have definitely been diagnosed with a neurodegeneration/demyelinating disease (multiple sclerosis have 3 patients, Lebeŕs optic neuropathy 1 patient, Parkinsoń disease 1 patient and Allgrove syndrome). Furthemore, 7 patients with positive questionnaire have been diagnosed with other neurological diseases (tetany, carpal tunnel syndrome, epilepsy). A total of 38 patients with positive questionnaires are still awaiting MR examination. In addition, 14 patients (27.4%) of those 51 patients with the presence of neurological symptoms (vs. 0 from 89 patients without any neurological symptoms) have positive family history of a neurodegenerative or a demyelinating disease.
**Conclusion:** Our preliminary results show an increased prevalence of at least 4.3% of neurodegenerative/demyelinating diseases in patients with achalasia (vs. approx. 1.4% in the Czech controls) and also a high prevalence of these disorders in family history.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0983 CONCURRENT AUTOIMMUNE DISEASES AND ASSOCIATED FACTORS IN PATIENTS WITH AUTOIMMUNE GASTRITIS

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**Introduction:** Autoimmune gastritis (AIG) is an autoimmune and inflammatory disorder of the oxyntic mucosa characterized by autoantibodies directed against structures containing $H^+/K^+$-ATPase and intrinsic factor, with subsequent loss of parietal cells. Autoimmune gastritis may be associated with other organ-specific autoimmune disorders, but the prevalence of this association is not entirely quantified.
**Aims & Methods:** The aims of this study were to investigate the prevalence of autoimmune disorders and evaluate the factors that might affect this association in patients with autoimmune gastritis. 320 patients with autoimmune gastritis were retrospectively studied and data on concomitant autoimmune diseases, serum gastrin and chromogranin A levels, Anti Hp IgG, antiparietal cell antibodies, presence of enterochromaffin cell hyperplasia and gastric atrophy were gathered for each patient and associations between autoimmune gastritis and studied parameters were explored through descriptive statistics and logistic regression analysis.
**Results:** Of the 320 atrophic body autoimmune gastritis patients, 171 (53.4%) had an associated autoimmune disorder. Autoimmune thyroiditis was the most common concurrent disease, diagnosed in 116 patients (36.2%). Multivariate analysis showed that, presence of enterochromaffin cell hyperplasia (odds ratio [OR] 9.445, 95% confidence [CI], 4.42–20.22) serum gastrin (OR 3.1, 95% CI. 1.46–6.60) and serum chromogranin A (OR 4.14, 95% CI, 2.01–8.52) levels remained significantly associated with the coexistence of an autoimmune disease.
**Conclusion:** Concurrent autoimmune diseases are common in patients with autoimmune gastritis. Autoimmune thyroiditis is the most encountered disease. These data suggest that patients with autoimmune gastritis should be investigated for the presence of an autoimmune disease, in particular patients with enterochromaffin cell hyperplasia and those with serum gastrin and chromogranin A levels above cut-off values.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0984 EFFECT OF INTRAGASTRIC FAT INFUSION ON THE GENERALIZATION OF REWARD SENSITIVITY


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**Introduction:** We have previously shown that subliminal intragastric infusion of a small amount of medium chain fatty acids influences eating behavior. It is unknown whether the reward sensitivity to an exteroceptive sensory stimulus can be generalized from one domain to another domain. Thus interoceptive sensory stimulus such as intragastric fat infusion might also influence reward sensitivity within and across domains.

**Aims & Methods:** Aim of the study: To explore whether the interoceptive sensory stimulus from the food domain will generalize the exteroceptive reward sensitivity within the food domain, and in the financial domain in healthy males. Methods: Fifty nine healthy heterosexual male were recruited for this counterbalanced 2-visit study. On each study day, subjects came to the lab after an overnight fast. A feeding tube was inserted in to the fundus of the stomach via the nose. After a 10-minutes adaptation period, they were lead to a computer for an online survey (Qualtrics, Provo, Utah, USA). Hunger rating and unpleasant feeling from the tube (visual analogue scale) were obtained via the survey, after which either 2.5 g lauric acid emulsified with 250 mL phosphate buffered water (350 mOsm/L) or physiological saline was infused within 2 minutes in each visit. From the start of the infusion, subjects were shown a neutral film with landscape for 10 minutes as a filler. At the end of the film the feeding tube was removed and another hunger rating was obtained via the survey. Subjects were then shown 10 high caloric and 10 low caloric food pictures in a random order, which they needed to rate on a 7-point scale "How much would you like to eat this food right now?", with end points 'totally not' and 'certainly yes'. Next, subjects completed an intertemporal discounting task in which they specified how much money they would require in one week, one month, three months, six months and one year, instead of receiving 15 euro now, using the standard instructions in a fixed order. Area under the discounting curve (AUC) was calculated as a measure of subjects' impatience for receiving smaller-sooner amount of money. Lastly, subjects were asked to guess what they were administered intragastrically (fatty acids or saline). We treated the AUC, and ratings of food picturesas dependent variables, and fat versus saline condition as within subject factor for the analysis. Moreover, we included subjects' absolute change in hunger feelings (after – before infusion) as covariate in our mixed model in SAS 9.2.

**Results:** 21 out of 59 subjects gave a wrong post hoc guess about the content of the intragastrically infused substance. Subjects with incorrect guess gave lower discounting rate after fat infusion compared to saline, while this effect didn't exist in the correct estimation group ($p = 0.02$, $p = 0.32$, respectively, mixed model). Furthermore the discounting rate increases in the incorrect estimation group, and decreases in the correct estimation group when the change of hunger rating is larger ($p = 0.02$, $p = 0.02$, respectively). In addition, regardless of the post hoc estimation, subjects' ratings to both high caloric and low caloric food were lower after fat infusion, even after controlling for the unpleasant feeling of the tube ($p = 0.04$, $p = 0.04$, respectively).

**Conclusion:** A subliminal sensory stimulus from the food domain decreases financial discounting rate, and this effect vanished if the sensory stimulus reached conscious level. The interoceptive stimulus of intragastric fatty acid decreases the sensitivity to exteroceptive food cues.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0985 RELATIONS AMONG AUTONOMIC NERVE FUNCTION AND GASTRIC EMPTYING IN PATIENTS WITH AUTOIMMUNE GASTRITIS


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**Introduction:** Autoimmune gastritis (AIG) is an autoimmune and inflammatory disorder of the oxyntic mucosa characterized by autoantibodies directed against structures containing $H^+/K^+$-ATPase and intrinsic factor, with subsequent loss of parietal cells. Signs of autonomic nervous system dysfunction exist in patients with autoimmune diseases between 24% and 100%. Some of the patients with AIG may have delayed GE causing upper gastrointestinal (GI) symptoms and this situation may be related to autonomic nerve dysfunction.

**Aims & Methods:** The purposes of this study were: (i) to define whether the autonomic nervous system dysfunction exists and determine the frequency and characteristics of dysautonomia in patients with AIG, (ii) to evaluate the association of autonomic nerve function characteristics with of GE based on radionuclide GE studies in patients with AIG. 75 patients (50 women, mean age $56.73 \pm 11.77$) diagnosed as having autoimmune gastritis were investigated by means of autonomic nervous system and gastric emptying tests. All patients underwent a standardized scintigraphic gastric emptying study and five tests evaluating autonomic nervous system. Patients with autonomic nervous system dysfunction were then analyzed and compared by means of existence of delayed gastric emptying and gastrointestinal symptoms.

**Results:** 62 patients had autonomic nervous system dysfunction (14 mild, 40 moderate and 8 severe autonomic dysfunction. The mean total score of autonomic tests was $3.85 \pm 2.35$. Total autonomic score of patients ($n = 60$) with delayed gastric emptying was significantly higher than patients ($n = 15$) with normal gastric emptying ($4.68 \pm 1.7$ vs.$1.53 \pm 0.58$, $p < 0.001$). Mean gastroparesis cardinal symptom index was significantly higher in patients ($n = 60$) with delayed gastric emptying half-time compared to patients ($n = 15$) with normal gastric emptying half-time ($1.89 \pm 1.16$ vs $0.4 \pm 0.3$, $p < 0.001$).

**Conclusion:** Most of patients with autoimmune gastritis have autonomic nerve dysfunction. There is a close relation between autonomic nervous system dysfunction and delayed gastric emptying. Gastroparesis cardinal symptom index has a high sensitivity and specifity in predicting both autonomic nerve function and delay in gastric emptying.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P0986 DETAILED ANALYSIS OF A SINGLE U.S. CENTER EXPERIENCE WITH PERORAL ENDOSCOPIC MYOTOMY (POEM) SUGGESTS ITS EFFICACY AND SAFETY WITH SIGNIFICANT OCCURRENCE OF POST-PROCEDURAL GASTROESOPHAGEAL REFLUX

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**Introduction:** POEM was introduced as a new effective therapeutic option for esophageal achalasia and other spastic esophageal disorders. It is currently believed that POEM is associated with low rates of post-procedural reflux and formal esophageal acid exposure testing is rarely performed after POEM.

**Aims & Methods:** To report outcomes of POEM performed by a single gastroenterologist at a single US center, including procedural adverse events (AEs) and gastroesophageal reflux (GER). Methods: All patients who underwent POEM at our institution were included. Clinical response was defined by decrease in Eckardt score to $\leq$3. AEs were graded according to the ASGE lexicon's severity grading system.

**Results:** A total of 104 patients (mean age 49.5 y, 48 females) underwent POEM from 11/2011 to 10/2015 for the treatment of achalasia (type I 10, type II 69, type III 15) or spastic esophageal disorders (n = 10) (table 1). POEM could not be completed in 1 patient due to extensive submucosal fibrosis resulting from prior therapies. The mean length of the procedure was 81.4 min (range 22–210) (table 2). The mean myotomy length was 11.6 cm (esophageal 8.3 cm, cardia 3.3 cm). A total of 83 (79.8%) patients underwent anterior myotomy while the remainder underwent posterior myotomy. The median length of hospital stay was 1.7 days (range 1–13). Among 75 patients with mean follow up period of 407 days (range 21–1447), clinical response was observed in 63 patients (84%) (86.6% vs. 62.5%, achalasia group vs. spastic disorders group, $p = 0.08$). There was significant decrease in Eckardt score after POEM (7.8 vs. 1.7, $p < 0.0001$). The mean lower esophageal sphincter (LES) resting pressure (mmHg) and the residual LES pressure (mmHg) decreased significantly after POEM (41.8 vs. 22.4, $p < 0.0001$ and 26.6 vs 11.5, $p < 0.0001$). A total of 16 adverse events occurred in 13 (12.5%) patients (5 mucosotomies, 2 pneumoperitoneum, 2 pneumothorax, 1 pulmonary embolism) (table 2): 13 complications were rated as mild, 3 moderate, and none severe. All mucosotomies were successfully treated with endoscopic closure. PH-impedance testing was completed in 47 patients following POEM: 32 (68.1%) had abnormal acid exposure with a mean De-Meester score of 81.53. Positive symptoms correlation was present in only 30% of patients.

**Conclusion:** POEM was successfully completed in 99% of the cases, even when extended indications (extremes or age, previous interventions, or sigmoid esophagus) were used. Adverse events were infrequent (12.5%) and could be managed intraprocedurally. There were no mortalities. Significant improvements in Eckardt scores and LES pressures were seen. However, post-POEM GER occurs in two thirds of patients and is most commonly silent. We, therefore, recommend formal esophageal acid exposure testing in all patients after POEM to avoid long-term complications due to caustic acid injury.

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## P0987 DOES ESOPHAGEAL ENDOSCOPIC RESECTION IMPAIR ESOPHAGEAL MOTILITY? – A PROSPECTIVE STUDY USING HIGH RESOLUTION MANOMETRY

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**Introduction:** Although endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) to early esophageal cancers has been performed widely, esophageal stenosis after ESD could lead dysphageal symptoms and result in decreasing quality of life [1][2]. Esophageal stenosis may impair esophageal motility, however there has been no study regarding whether EMR/ESD would affect esophageal motility so far.

**Aims & Methods:** The aim of this study is to evaluate the esophageal motility using high-resolution manometry (HRM) before and after EMR/ESD, prospectively. Patients who scheduled to undergo endoscopic therapy of esophageal tumor were prospectively enrolled. Symptom score evaluation (Eckardt score, Dysphagia score) and HRM (Star Medical, Inc, Tokyo, Japan) was performed before and after endoscopic resection(ER). Based on Chicago classification as categories of esophageal motors dysfunction [3], HRM results are expressed as DCI; Distal Contractile Integral(>20.0) (mHg-cm-s), CFV; Contractile Front Velocity (cm/s), IBP; Intrabolus Pressure (mmHg), IRP; Integrated Relaxation Pressure (mmHg), DL; Distal Latency (sec). We divided patients into two groups, patients who underwent more than 2/3 circumference resection (group A) and less than 2/3 circumference resection (group B). This study was approved by the ethical committee. (UMIN Clinical Trials Registry: UMIN000015829)

**Results:** Out of 27 enrolled patients, 22 patients (male/female; 17/5, mean age; 66, range; 52–80) were able to be analyzed (group A: 11, group B: 11). Symptom scores worsened in 72.7% of group A, but not in group B. Result of HRM were, DCI (beforeER/ afterER): ($1462 \pm 1144$/ $2104 \pm 1615$) ($p < 0.05$), CFV: ($5.3 \pm 2.5$/ $3.6 \pm 0.5$) (p: 0.08), IBP: ($4.8 \pm 6.7$/ $4.0 \pm 6.9$), IRP: ($7.5 \pm 5.6$/ $10.3 \pm 7.7$), DL: ($6.7 \pm 1.9$/ $7.6 \pm 0.8$) in group A, respectively. DCI: ($2322 \pm 1145$/ $2583 \pm 1517$), CFV: ($4.6 \pm 2.0$/ $4.6 \pm 2.2$), IBP: ($7.1 \pm 6.8$/ $8.6 \pm 8.0$), IRP: ($12.9 \pm 7.9$/ $11.2 \pm 7.2$), DL: ($6.9 \pm 1.0$/ $6.9 \pm 0.6$) in group B, respectively.

**Conclusion:** There were no significant differences of esophageal motility before and after esophageal endoscopic resection in group B. However, significant increase of DCI and tending to decrease of CFV was observed in group A indicating that massive esophageal endoscopic therapy impaired esophageal motility.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0988 DELAYED GASTRIC EMPTYING IS ASSOCIATED WITH INCREASED RISK OF CARDIOVASCULAR DISEASE INDEPENDENT OF THE AETIOLOGY OF GASTROPARESIS

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**Introduction:** Patients with diabetic gastroparesis have an increased risk of cardiovascular disease (CVD) which is partly attributed to autonomic neuropathy as a common risk factor. Moreover, diabetics have decreased ghrelin secretion which also has been shown to influence both, gastric emptying velocity and the risk of CVD. It is unknown, whether – independent of the aetiology of gastroparesis – there is an association between gastroparesis and CVD and whether autonomic neuropathy and decreased ghrelin release may be of pathophysiological importance.

**Aims & Methods:** This prospective study aimed to investigate the association between gastric emptying (GE), cardiovascular risk, autonomic neuropathy and ghrelin release. Patients with symptoms compatible with gastroparesis underwent a standardized $^{13}$C-octanoic acid breath test for calculation of GE half time (T½) and cumulative $^{13}$C-exhalation, measurement of ghrelin release in response to the test meal, heart rate variability (HRV) measurements and rigorous evaluation of cardiovascular risk factors to calculate the probability of a major cardiovascular event during the next 10 years (CVR) using evaluated software.

**Results:** 83 patients (59 females) participated, including 15 diabetics. In 5 patients GE was accelerated (T½ < 50 min), in 19 delayed (T½ > 150 min). The probability for a major cardiovascular event was significantly different in patients with accelerated (CRV, mean±SD: 0.8 ± 0.7%), normal (12.4 ± 17.4%) and delayed (24.2 ± 20.3%) GE ($p = 0.004$). Reduced HRV correlated with slower GE ($p < 0.019$), and 4 out of 5 patients with severely delayed GE (T½ > 250 min) had HRV results compatible with manifest autonomic neuropathy. Only 2 of these were diabetics. Postprandial ghrelin release correlated directly with HRV ($p = 0.034$) and inversely with GE time ($p = 0.006$). Multiple linear regression analysis revealed that, of commonly accepted risk factors for CVD (including diabetes), only male sex was an independent risk factor for reduced ghrelin release.

**Conclusion:** Not only patients with diabetic gastroparesis, but also with other aetiologies have an increased risk for CVD. This might partly be explained by autonomic neuropathy and/or reduced ghrelin release. Moreover, increased prevalence of CVD might contribute to the increased mortality rate in gastroparesis shown before (1). Further studies are needed to clarify whether a diagnosis of gastroparesis should trigger the search for CVD, also in non-diabetic patients.

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All other authors have declared no conflicts of interest.

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## P0989 COMPARISON BETWEEN ANTERIOR AND POSTERIOR MYOTOMY DURING PERORAL ENDOSCOPIC MYOTOMY FOR TREATING ACHALASIA: A RANDOMIZED, PROSPECTIVE STUDY

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**Introduction:** Peroral endoscopic myotomy (POEM) has been demonstrated to be safe and effective for treating achalasia. Though most groups perform POEM on the anterior wall of the esophagus with patients in the supine position, some groups perform it on the posterior wall with patients in the left lateral position. However, little is known about the comparison between the two different methods of POEM.

**Aims & Methods:** Aim: To compare the safety and efficacy of anterior myotomy and posterior myotomy for the treatment of achalasia. Methods: From August 2015 to January 2016, a total of 30 consecutive achalasia patients without prior treatment or sigmoid-type esophagus were prospectively recruited. They were randomized into anterior or posterior group. Clinical data about general characteristics, operative parameters, pre- and postoperative Eckardt score, esophageal manometry results, 24-hour PH test, adverse events were collected and compared between the two groups.

**Results:** There are 15 patients in each group, and all of them underwent POEM successfully. The mean operation time was significantly shorter in posterior group compared with the anterior group (41.3 ± 12.0 min vs. 49.7 ± 8.8 min, $P < 0.05$). Treatment success (defined as an Eckardt score ≤3) was achieved in 100% of the 30 patients during a median follow-up of 6 months (3∼8 months). Mean Eckardt score decreased significantly from 6.3 ± 1.5 (baseline value) to 0.7 ± 0.6 ($p < 0.001$). Postoperative mean basal LES pressure and 4sIRP were significantly lower compared to the preoperative values (39.3 ± 6.7 mmHg and 29.1 ± 5.5 mmHg vs 14.3 ± 3.8 mmHg and 10.4 ± 2.8 mmHg, respectively, $p < 0.01$). Adverse events were seen in 13.3% (4/30) of the cases, namely 1 subcutaneous emphysema in the posterior group, and 1 subcutaneous emphysema and 2 arrhythmia (nodal tachycardia and supraventricular tachycardia) in the anterior group. The 2 subcutaneous emphysema was spontaneous absorbed within 3 days without additional intervention. The arrhythmias were seen on the monitor during myotomy procedure and it returned to normal sinus rhythm after myotomy completed. There was no significant difference between the 2 groups in terms of treatment success, pre- and postoperative esophageal manometry, Eckardt score and adverse events ($P > 0.05$).

**Table 1:** Comparison of characteristics between the two groups

| | Anterior myotomy (n = 15) | Posterior myotomy (n = 15) | P |
|---|---|---|---|
| Sex, M/F | 7/8 | 5/10 | 0.710 |
| Age, year | 44.3 ± 13.9 | 41.9 ± 13.4 | 0.634 |
| Disease course, year | 5.1 ± 4.8 | 4.3 ± 4.7 | 0.574 |
| Achalasia type, I/II/III | 2/13/0 | 1/13/1 | 0.513 |
| Pre-POEM Eckardt score | 6.3 ± 1.5 | 6.1 ± 0.8 | 0.655 |
| Pre-POEM LESP, mmHg | 41.6 ± 8.0 | 38.8 ± 6.7 | 0.218 |
| Pre-POEM 4sIRP, mmHg | 29.6 ± 4.7 | 28.2 ± 5.4 | 0.421 |
| Operative time, min | 49.7 ± 8.8 | 41.3 ± 12.0 | 0.021 |
| Complications | 20% (3/15) | 6.7% (1/15) | 0.315 |
| Subcutaneous emphysema | 6.7% (1/15) | 6.7% (1/15) | 1.000 |
| Arrhythmia | 13.3% (2/15) | 0% (0/15) | 0.483 |
| Hospital stay, day | 4.8 ± 0.6 | 5.1 ± 1.1 | 0.391 |
| Follow-up, month | 6 (3∼8) | 6 (3∼8) | 0.941 |
| Post-POEM Eckardt score | 0.73 ± 0.59 | 0.67 ± 0.61 | 0.765 |
| Post-POEM LESP, mmHg | 15.8 ± 3.8 | 13.6 ± 3.7 | 0.198 |
| Post-POEM 4sIRP, mmHg | 11.2 ± 3.3 | 10.0 ± 2.5 | 0.335 |
| GERD symptom, % | 13.3% (2/15) | 20% (3/15) | 1.000 |
| PH test, % | 26.7% (4/15) | 33.3% (5/15) | 1.000 |
| Esophagitis, % | 13.3% (2/15) | 13.3% (2/15) | 1.000 |

**Conclusion:** The treatment efficacy and manometry outcomes were comparable between the two groups, but a posterior myotomy could reduce the procedure time. Although the overall adverse events were comparable, arrhythmia may be seen during POEM in the anterior group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0990 ABNORMAL INTRA-BOLUS PRESSURE CORRELATES WITH ESOPHAGO-GASTRIC DYSFUNCTION AND WITH INCREASING AGE – A STUDY USING HIGH-RESOLUTION MANOMETRY

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**Introduction:** High-Resolution Manometry (HRM) is currently considered the gold standard to assess esophageal peristalsis and esophago-gastric junction (EGJ) function. Indeed, with the use of this technology novel validated metrics have been developed to define clinically relevant esophageal motility abnormalities. On the other hand, among these novel metrics, there are few features whose interpretation and utility are still challenging. In particular, the intrabolus pressure (IBP) has been initially regarded as an indirect measure of bolus transit trough the EGJ.
**Aims & Methods:** We aimed to investigate the frequency of abnormal IBP and the factors implicated in its development in consecutive patients with esophageal symptoms. We included consecutive patients with esophageal symptoms (i.e. heartburn, regurgitation, dysphagia, non-cardiac chestpain) referring to our motility laboratory. Patients with gastro-intestinal surgery, achalasia or scleroderma were excluded. All patients underwent esophagogastroduodenoscopy off-antisecretory drugs (discontinued at least 30 days before the endoscopy) to assess the presence of esophageal mucosal lesions and HRM with 5-min baseline recording and 10 single water swallows. The diagnostic criteria for manometry agreed with the Chicago Classification vers. 3. We stratified these patients according to their IBP value (i.e. abnormal if $\geq$ than 17 mmHg according to literature) in two groups: patients with normal and those with abnormal IBP values. Data were expressed as mean and standard deviation. A t-test and x2-test were performed and a p-value $<0.05$ was considered statistically significant.
**Results:** Overall 200 patients (95 Male/105 Female, $56 \pm 15$ years) with esophageal symptoms were enrolled ($n = 80$ with heartburn, $n = 30$ with regurgitation, $n = 40$ with dysphagia, $n = 50$ with non-cardiac chestpain). Abnormal IBP is quite common in patients with dysphagia and non-cardiac chestpain, whereas is less frequent in patients with heartburn and/or regurgitation ($p < 0.05$). Patients with abnormal IBP had a mean age higher than patients with normal IBP ($60 \pm 13$ vs $50 \pm 16$; $p < 0.001$), but no difference was found in terms of gender distribution and BMI ($p = ns$). As to HRM characteristics, patients with abnormal IBP had similar mean Distal Contractile Integral (DCI) than those with normal IBP ($2287 \pm 10538$ vs. $2100 \pm 1497$; $p = 0.9$), but a lower esophageal sphincter (LES) resting pressure ($22 \pm 11$vs $33 \pm 16$; $p < 0.001$) and an increased IRP ($22 \pm 11$vs$33 \pm 16$; $p < 0.001$). No differences were found in terms of distal latency ($6.7 \pm 1.5\%$ vs $6.4 \pm 2.0\%$; $p = 0.14$), peristaltic swallow ($70 \pm 34\%$ vs $78 \pm 27\%$; $p = 0.07$), abnormal type of swallow such as failed, ineffective, and fragmented ($p = ns$) and EGJ morphologies ($p = ns$).
**Conclusion:** Patients with abnormal IBP values presented an increased IRP and LES resting pressure compared to patients with normal IBP values, suggesting that a reduced EGJ compliance may play an important role in its determination. Further, we observed that IBP values increase with ageing and this phenomenon could be explained by the anatomic and functional alterations age-related. Further studies investigating the diagnostic and pathogenetic role of abnormal IBP are required.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0991 POSTPRANDIAL INTRAGASTRIC PH LEVELS ARE ELEVATED FOR SIGNIFICANTLY LONGER ON REFLUX MONITORING IN PATIENTS WITH CONFIRMED GASTROPARESIS

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**Introduction:** Many patients present to gastroenterology services with multiple upper GI symptoms. Complaints of postprandial retrosternal/epigastric discomfort with regurgitation are common and can suggest gastro-oesophageal reflux disease, gastroparesis, or both. Disentangling the differentials can be difficult on clinical history alone. The need for several tests to exclude each diagnosis has cost and time implications for clinicians and patients. It is known that intragastric pH rises from baseline ~1 to a median of 4.5 during a meal and gradually returns to fasting-state as the buffer (i.e ingested food) leaves the stomach. We aimed to establish if reflux monitoring, where intragastric pH is recorded routinely, could also detect longer periods of high pH postprandially in subjects with confirmed gastroparesis compared to those with normal gastric emptying.
**Aims & Methods:** From our database of patients seen in our tertiary referral GI physiology unit, we identified patients with confirmed delayed gastric emptying on $^{13}$C-octanoic acid breath test from 2009–2015 who had also undergone 24-hour reflux monitoring off PPI (combined pH-impedance). Another group of symptomatic patients with normal gastric emptying times on breath test, who also had reflux monitoring, were identified as controls. We interrogated reflux monitoring traces for baseline fasted pH, then measured the time taken for intragastric pH to return to baseline from the end of self reported mealtimes. Median times for return of postprandial intragastric pH to baseline were compared between groups.
**Results:** 57 eligible patients with gastroparesis (38 female, age range 13 to 70 years, median 39) were identified and compared with 45 subjects with normal gastric emptying times (32 female; age range 18–72, median 45 years). Median baseline fasting intragastric pH in those with normal gastric emptying and gastroparesis was 1.2 and 1.3 respectively. The median duration for postprandial intragastric pH to return to baseline for the control group was 62 minutes (95% CI: 51–70 min) compared to 109 min for the gastroparesis group (95% CI: 74–127). The difference between the two groups was significant ($p = 0.0002$).
**Conclusion:** Intragastric pH is elevated for longer periods postprandially in patients with gastroparesis. The intragastric pH data readily captured on reflux monitoring can be useful to identify patients with simultaneous pathological reflux and delayed gastric emptying. A prospective sudy where $^{13}$C-octanoic acid breath testing using standardised meal is performed with concurrent reflux monitoring is currently underway at our unit.
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## P0992 MANAGEMENT OF RECURRENT SYMPTOMS AFTER PERORAL ENDOSCOPIC MYOTOMY IN ACHALASIA

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**Introduction:** Peroral endoscopic myotomy (POEM) has been rapidly gaining ground as a treatment for achalasia. Although POEM is a safe and effective treatment, a subset of patients has persistent or recurrent symptoms after POEM. It is currently not known how these patients can be managed best.
**Aims & Methods:** This study aimed to examine the efficacy of different retreatments after failed POEM and to identify predictors of retreatment success. In three tertiary care hospitals in Europe and the USA all achalasia patients with recurrent or persistent symptoms after POEM (Eckardt symptom score $>3$) were identified between 2011 and 2015. Retreatment success was defined as an Eckardt score $\leq 3$ persisting for at least six months. Retreatment failure was defined as Eckardt $>3$, also if patients developed recurrent symptoms after a symptom-free period.

**Abstract No: 0993**

**Table 1:** Main HRM results and statistical analisys (ANOVA and Bonferroni tests).

| | Percentage of failed swallows | | | | | p |
|---|---|---|---|---|---|---|
| | Group A (17) ≤30% | Group B (11) 40% | Group C (10) 50% | Group D (8) 60% | Group E (8) ≥70% | |
| Mean age (IQR) | 44.5 (16.2) | 43.2 (16.8) | 51.3 (7.2) | 39.8 (13.6) | 47.1 (18.1) | 0.57 |
| **P > 0.05 for all pairwise comparisons** | | | | | | |
| DCI mean (IQR) | 1255.5 (577.8) | 1466 (623.5) | 1153 (577) | 598 (582) | 284 (235) | 0.0001 |
| **P < 0.001 between A vs D; A vs E; B vs D; B vs E; C vs D and C vs E** | | | | | | |
| DCI-MRS (IQR) | 1653 (541.8) | 1578 (502) | 1241 (828) | 472 (507) | 119 (221) | 0.0001 |
| **P < 0.001 between A vs D; A vs E; B vs D; B vs E; C vs D and C vs E** | | | | | | |
| MRS/WS ratio (IQR) | 1.3 (0.6) | 1.1 (0.2) | 1.1 (0.3) | 0.6 (0.6) | 0.5 (0.3) | 0.0001 |

P < 0.001 between A vs D; A vs E; B vs D; B vs E; C vs D and C vs E

**Results:** From a cohort of 441 patients that underwent POEM, we identified 43 achalasia patients (14 females; mean age 42 years, range 17–84) with an Eckardt >3 after POEM. Before POEM, most patients had either received no treatment (22 patients; 51%) or endoscopic dilatations (17 patients; 40%). Median relapse time of symptoms after POEM was 6 months (IQR 3–20). The majority of patients (34 patients; 79%) received one or more retreatments after POEM. The other nine patients started a modified diet or refused treatment. Overall, in 17 patients (50%), the final retreatment was effective for at least six months, but efficacy differed for the choice of treatment. Laparoscopic Heller myotomy was effective in 45% of patients, and re-POEM in 63% of patients. Pneumatic dilatation (PD) with a 30 mm balloon was never long-term effective, PD 35 mm was effective in 22% of patients. When PD 35 mm was not effective, PD 40 mm also was not effective. No complications of retreatments occurred. On univariate logistic regression, patients with successfull retreatment were more often female patients ($p = 0.038$) and had a higher initial Eckardt score ($p = 0.041$), compared to patients with failed retreatment.

**Conclusion:** In our cohort of patients with POEM failure, laparoscopic Heller myotomy and re-POEM showed a modest efficacy, whereas pneumodilatation showed a poor efficacy.

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## P0993 WHICH IS THE BEST CUT-OFF TO DEFINE INEFFECTIVE ESOPHAGEAL MOTILITY?

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**Introduction:** The last version (3.0) of Chicago Classification took anarbitrary decision and defined ineffective esophageal motility (IEM) when 50% or more wet swallows (WS) result failed (DCI < 100 mmHg/cm/s) or weak (100 < DCI < 450 mmHg/cm/s) during standard manometric protocol.

**Aims & Methods:** The aim of this study was to compare patients with different frequency of failed/weak WS, provocative test (MRS, 3 ml x 5times in 10 sec) and MRS/WS ratio to better define the IEM diagnosis. We retrospectively evaluated 59 outpatients who underwent: upper endoscopy, high-resolution manometry (HRM) with 5-min baseline recording, 10 single water swallows of 5 mL each, and 1 MRS in supine position, and 24-h impedance and pH monitoring for unresponsive heartburn. We excluded patients with achalasia, scleroderma, absent peristalsis and prior surgery. MRS/WS ratio was calculated according to medical literature. All patients were sub-grouped based on the percentage of failed/weak WS as follows: a) ≤30%; b) 40%; c) 50%; d) 60% and e) ≥ 70% failed or weak WS. All data were expressed in median and IQR. ANOVA with Bonferroni test has been applied for statistical analysis.

**Results:** Male were more represented in groups C (60%), D (75%), E (75%) ($p = 0.03$), whereas mean age was similar in all groups ($p = 0.57$). Erosive esophagitis was more represented in groups C (70%), D (50%), E (50%) ($p = 0.018$). Acid exposure time increased progressively from group A to E (A 4.3 [IQR 5.6]; B 8.2 [8.4]; C 9 [5.7]; D 9.1 [11.3]; E 10.2 [7.4]; $p = 0.014$). Total number of reflux events was higher in C and D groups (A 45.3 [IQR 20.7]; B 49 [85]; C 96 [71]; D 80 [37.5]; E 57.5 [76.7]; $p = 0.008$). Mean DCI during WS, DCI-MRS and MRS/WS ratio were progressively lower from A to E group ($p < 0.001$ with ANOVA). The Bonferroni test showed significant differences between A, B, C, versus D and E ($p < 0.001$). Details are reported in table 1.

**Conclusion:** Data on GERD evidence at impedance-pH monitoring demonstrated that IEM should be considered as clinically relevant when the frequency of failed or weak WS is ≥60%.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P0994 DEVELOPMENT AND VALIDATION OF AN ENDOSCOPY-BASED ACTIVITY INDEX FOR ADULTS WITH EOSINOPHILIC ESOPHAGITIS

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**Introduction:** The recently published grading and classification system for eosinophilic esophagitis (EoE) evaluates the presence and severity of exudates, rings, edema, furrows, and strictures (EREFS). To date, the score for the EREFS grading system has not been developed.

**Aims & Methods:** We aimed to develop and validate an endoscopic score based on the EREFS system. Adult EoE patients in Switzerland and the United States underwent esophagogastroduodenscopy. The endoscopists recorded the severity of EoE-associated endoscopic features in accordance with the EREFS system. Five expert endoscopists reviewed the grading of EoE-associated endoscopic features and provided an Endoscopist Global Assessment (EndoGA) of endoscopic EoE activity (on a Likert scale from 0 to 10). In order to develop a score based on EREFS grading system, linear regression was used to quantify the way mean of EndoGA provided by five experts varied with the severity of endoscopic features. The regression based score was developed in a group of 153 adult patients with EoE (72.5% male, median age, 38 years) and validated in an independent group of 120 EoE patients (60.8% male; median age, 40.5 years).

**Results:** The mean of the difference between the highest and the lowest EndoGA rating provided by the five expert endoscopists for a given patient was 2.5 (IQR 1.0–3.6, range 0–6.5); white exudates contributed most to differences in EndoGA ranking among expert endoscopists. In the EREFS-based score, variations in severity of endoscopic features explained 92% of the EndoGA variability. The predicted EndoGA increased most, if patient had severe rings (regression coefficient of 2.5) and severe white exudates (coefficient of 3.0), and least, if patient presented with furrows (coefficient of 0.7). In the validation patients, the mean difference between EndoGA and EREFS score

was 0.13. The proposed EREFS based score ranges from 0 to 9 with various EoE-associated features graded as follows: edema (absent = 0, present = 1), rings (absent = 0, mild = 1, moderate = 2, severe = 2.5), white exudates (absent = 0, mild = 1, severe = 3), furrows (absent = 0, present = 0.5); strictures (absent = 0, low-grade = 1, intermediate-/high-grade = 2).
**Conclusion:** For a given set of endoscopic features, endoscopists differ with respect to overall impression of endoscopic disease activity with white exudates being the source of most inconsistencies in EndoGA ranking among experts. We developed and validated an EoE endoscopy score based on the EREFS grading and classification system. The utility of the score for the purposes of observational studies and clinical trials needs to be further evaluated.gov number, NCT00939263.
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## P0995 LOW INCIDENCE OF EOSINOPHILIC OESOPHAGITIS. DO WE STILL LACK AWARENESS?

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**Introduction:** Eosinophilic oesophagitis (EO) has emerged as a leading cause for dysphagia and food bolus. Expert consensus recommends that oesophageal biopsies be taken in all those who present with these symptoms, where no other cause is identified at endoscopy.
**Aims & Methods:** The aim of this study was to assess the incidence of EO in this group and review the frequency of oesophageal biopsies in accordance to this guidance.
All index gastroscopies undertaken for dysphagia or food bolus, from September 2014 to September 2015 at our trust, were retrospectively analysed. Patient demographics, endoscopic diagnosis, frequency of oesophageal biopsies in a normal oesophagus or suspected EO cases and the incidence of EO were noted.
**Results:** A total of 1017 cases fulfilled the inclusion criteria (97% dysphagia and 3% food bolus). Incidence of cancer was 6% (n = 59), with further causal oesophageal pathology identified in 41% (n = 416). In the 53% (n = 542) of cases with a normal oesophagus, biopsies were only taken in 10% of cases (n = 56) and in 20% (n = 6) of food bolus patients. The incidence of EO was 6.8% (n = 13) in the biopsied group, giving an overall incidence of 1.3% for those who presented with dysphagia or food bolus. Median age of diagnosis for EO was 45 years (range 21–73) and 69% were male (n = 9). Only 6 cases were suspected endoscopically (Schatzki ring n = 2, stricture n = 1, furrows n = 3). 62% (n = 8) of EO patients had a history of atopy and 39% (n = 5) serum eosinophilia. Median duration of symptoms was 5 years (range 0.1–10yrs).
**Conclusion:** The overall incidence of EO in our study group was low compared to published literature, this is likely to be reflected by the low frequency of biopsies being undertaken in this at-risk group. Awareness in recognising endoscopic features of EO and the need for screening, through biopsy, in this cohort of patients' needs to be increased among all endoscopists.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0996 INFLUENCE OF FOUR DIFFERENT BIOPSY FORCEPS MODELS ON QUANTITY AND QUALITY OF EPITHELIAL AND SUBEPITHELIAL TISSUE SAMPLING IN EOSINOPHILIC ESOPHAGITIS

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**Introduction:** Eosinophilic esophagitis (EoE)-associated histologic alterations encompass the entire thickness of the esophagus including the subepithelial layer, which is not routinely sampled. As such, information about underlying subepithelial fibrosis that may impact esophageal compliance if often missing.
**Aims & Methods:** We evaluated four biopsy forceps models by assessing the following parameters: 1) success rate with which subepithelial tissue was sampled; 2) the amount of tissue biopsied; 3) quality of biopsy orientation; and 4) complications. The following forceps were used: static jaw (Olympus, FB-11K-1 and FB-45Q-1), alligator jaw (Olympus, FB-210 K), and large capacity (Boston-Scientific, Radial Jaw 4). One gastroenterologist took 240 esophageal biopsies from 30 adult EoE patients. One pathologist calculated the surface area of epithelial and subepithelial layers in H&E-stained biopsies.
**Results:** Subepithelial tissue was sampled with the following success rate: 96.7% (static jaw FB-11K-1); 92.5% (static jaw FB-45Q-1); 80% (alligator jaw); 55% (large capacity). The median ratios of the surface area of the epithelial to that of subepithelial tissue sampled were as follows: $2.05 \pm 2.52$ (static jaw FB-45Q-1); $2.56 \pm 4.96$ (static jaw FB-11K-1); $4.01 \pm 5.06$ (alligator jaw); and $5.83 \pm 7.25$ (large capacity). A larger surface area of subepithelial tissue was obtained using the static jaw forceps when compared to that using alligator jaw ($p < 0.001$ and $p = 0.037$) and the large capacity forceps ($p < 0.001$). When large capacity forceps were used, the highest rate of poorly oriented biopsies (27.5%) was observed. No esophageal perforations or hemorrhages occurred.
**Conclusion:** The static jaw forceps allowed to sample subepithelial tissue in >90% of biopsies and appear to be superior to alligator or large capacity forceps in sampling larger amount of subepithelial tissue. Sampling deeper biopsies is safe.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0997 EFFICACY OF TOPICAL STEROIDS IN EOSINOPHILIC ESOPHAGITIS: A METAANALYSIS

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**Introduction:** Eosinophilic esophagitis (EoE) is a chronic inflammatory allergen-mediated disease with increasing frequency. Recommend therapeutic options include elimination diets and topical steroids. The aim of this analysis was to determine the efficacy of topical steroids in the treatment of EoE based on recent randomized controlled trials.
**Aims & Methods:** We searched Pubmed and Embase for randomized controlled trials on topical steroids for treatment of active EoE fully published until 12/2015. Treatment effects were calculated as mean difference of eosinphil counts before and after treatment.
**Results:** 9 studies (budesonide n = 3, fluticasone n = 6) with a total of 416 Patienten were included. In placebo-controlled trials (n = 6) topical steroids were associated with a significant reduction of esophageal eosinophilc counts (standardised mean difference, SMD: −0.864 [−1.274, −0.454], $p < .001$). There was a moderate heterogenity between studies ((I^2 = 49.82%; Q(df = 5) = 9.86, p-val = 0.0793), which was mainly caused by differences in patient's age. There was no significant difference between budesonide und fluticasone trials (SMD = 0.389 [−0.437, 1.214], p = 0.3561). Placebo-controlled trials showed stronger effects than trials using PPI or prednisolone as comparator (p = 0.0021). The patient's age and gender had no significant influence on the efficacy of topical steroids.
**Conclusion:** Topical steroids are effective and well tolerated for the treatment of eosinophilic esophagitis independent of the patient's age and gender.
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All other authors have declared no conflicts of interest.

## P0998 EOSINOPHILIC OESOPHAGITIS: IMPROVING DIAGNOSIS AND OPTIMIZING THERAPY

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**Introduction:** Eosinophilic oesophagitis (EoE) is a chronic condition of the oesophagus characterized by a dense eosinophilic infiltrate defined as >15 eosinophils/high power field (eos/hpf). The aim of this study was to capture the prevalence of EoE in a tertiary referral centre in London, to identify factors associated with a positive diagnosis and interrogate optimal response to therapy.
**Aims & Methods:** From February 2013 to November 2015, all patients presenting with solid food dysphagia to University College Hospital had a high resolution white light endoscopy. Those with cancer, achalasia, postoperative stricture or endotherapy for Barrett's were excluded. Endoscopy, histology and clinical data were collected. >15oes/hpf were defined as positive for EoE. A separate histopathology search identified patients with >15eos/hpf and no dysphagia. A prospective follow-up was conducted in focusing on therapy and response in those with >15 eos/hpf.
**Results:** Out of the 1566 patients with dysphagia, 524 were excluded for reasons stated. 736/1042 (71%) had oesophageal biopsies. Of those, 67 (9.1%) had more than 15eos/hpf. Another 14 patients with >15eos/hpf with symptoms other than dysphagia were identified from histology records, making the total number with eosiniphilia 81. The mean number of biopsies taken in those with >15eos/hpf (6.3) was greater than those with <15eos/hpf (5.1; p = 0.003). EoE patients were more likely to be male (70%) and younger ($43 \pm 16$ years) compared to nonEoE (40% male, $p < 0.0001$; $59 \pm 16$ years, $p < 0.0001$). Typical endoscopic features were found in 39 (48%) EoE patients; rings/furrows in 26 (32%) and strictures in 15 (18%). 42/81 (52%) were treated with PPIs only of which 19 (45%) clinically responded. 18 (22%) patients had both PPI and topical steroids (12 had steroids after PPI failure) while 8/81 (10%) had steroids only. Clinically 14/26 (54%) responded optimally to topical steroids, 13 of which had dysphagia. Overall, response to steroids occurred in those with a higher eosinophilia (53 vs 24, p = 0.004) and all 9 with ≥40eos/hpf had a complete response. Furthermore, typical EoE findings at endoscopy was more likely to be associated with a poor response to PPIs ($p < 0.0001$).
**Conclusion:** A higher number of biopsies taken raises the diagnostic yield; however still up to 1/3 patients in a modern referral centre have no biopsies taken. EoE should be excluded in those with no dysphagia and refractory reflux symptoms. Although PPIs are provided as first-line therapy, a positive response to steroids is more likely in those with higher numbers eos/hpf, while those with

fewer numbers and no endoscopic features could be considered for PPI therapy first. Such findings might be a useful tool to help tailor therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P0999 SIX-FOOD ELIMINATION DIET EFFECTIVELY INDUCES AND MAINTAINS REMISSION IN ADULTS WITH EOSINOPHILIC OESOPHAGITIS

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**Introduction:** Adults present with eosinophilic oesophagitis (EoO) most frequently with food impaction and dysphagia, and due to growing evidence it is increasingly diagnosed.
**Aims & Methods:** Aims: To evaluate the efficacy of the 6-food elimination diet (SFED) in inducing and maintaining remission and identify clinical, demographic, histological and endoscopic findings in adults diagnosed with EoO. In addition, the study evaluated the efficacy of SFED in maintainance of remission in adults with EoO diagnosed in pediatric age. Methods: Clinical, demographic, histological and endoscopic findings were retrospectively analyzed before and after SFED (wheat, soy, nuts, seafood, egg and food with cow milk) in 27 adults (17 diagnosed at adult age, 10 pediatric cases) followed in a tertiary centre clinic.
**Results:** Most patients were male (83%) and 52% had an atopic background. Dysphagia or food impaction were th presenting symptom in 94% of patients. Furrowing was the only endocopic finding present in all cases. Skin testing and IgE levels did not identify food triggers in most patients. In 88% of cases SFED induced clinical and histological remission. Food with cow milk were the most frequently identified trigger (82%). Around 90% adults diagnosed in pediatric age maintained clinical and histological remission over time with SFED (median time follow up 3.5 years).
**Conclusion:** SFED induced clinical, endoscopic and histological remission in 88% of adults with EoO. Remission was maintained in adults diagnosed with EoO with SFED. SFED is an effective and long-lasting treatment option for adults with EoO.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1000 DIFFERENTIATION OF EOSINOPHILIC ESOPHAGEAL MYOSITIS FROM EOSINOPHILIC ESOPHAGITIS

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**Introduction:** Eosinophilic esophagitis (EoE) is a Th2-mediated allergic disease of the esophageal epithelium. We previously reported a case series for eosinophilic esophageal myositis (EoEM)—a novel eosinophilic gastrointestinal disorder (EoGID) as eosinophilic infiltration localized in the esophageal muscle layer.[1] EoEM was diagnosed by peroral endoscopic muscle biopsy (POEM-b), which is a new histopathological diagnosing method developed from peroral endoscopic myotomy (POEM).
**Aims & Methods:** Four patients (mean age $54.0 \pm 17.7$[SD] y; all men) were diagnosed with EoEM in our case series July 2014 through February 2016. In the same period, four other patients ($53.5 \pm 15.6$ y, 3 men) were diagnosed with EoE. The clinical features and histopathology of EoEM were investigated to differentiate it from EoE.
**Results:** Those patients with EoEM had suffered from medicine (calcium blockers and proton pump inhibitors)-resistant chest pain and dysphagia, and initially three were diagnosed with Jackhammer esophagus, and one with Nutcracker esophagus on high-resolution manometry (HRM). Conventional endoscopy and mucosal biopsy samples of the esophagus showed no characteristic findings (no eosinophils in the epithelium [maximum number, $0 \pm 0$/ high-power field [HPF]). Thereafter, POEM was performed to resolve the esophageal spastic contraction and POEM-b for histopathological assessment. In the muscle layer samples obtained by POEM-b, severe eosinophil infiltration was observed ($46.8 \pm 16.5$/HPF). In contrary, severe eosinophil infiltration ($38.5 \pm 11.3$/HPF) was observed in the esophageal epithelium of EoE. And HRM showed failed perstalsis in those patients with EoE.
**Conclusion:** Our study indicates that HRM is a useful tool to raise a first suspicion of EoEM. The EoEM histological pattern displays clear differences from that of EoE.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1001 THE PREVALENCE OF JOINT HYPERMOBILITY IN DIFFERENT PHENOTYPES OF REFLUX DISEASE: INCREASED IN OESOPHAGEAL HYPERSENSITIVITY

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**Introduction:** Joint hypermobility (HM) refers to increased flexibility of the joints which is present in 5–17% of the population, and is assessed by clinical examination or validated hypermobility questionnaire. HM is associated with gastro-oesophageal reflux (GOR) symptoms (1). The aim of the study was to determine the prevalence of joint hypermobility in a large number of well-phenotyped patients with symptoms of GOR disease.

**Aims & Methods:** A cross-sectional study of patients attending our GI physiology unit for investigation of reflux symptoms over 4 years was undertaken. Patients completed the validated joint hypermobility questionnaire; scores $\geq 2$ out of 5 represented HM (2). Information from gastroscopy and physiology testing was used to determine whether patients had pathological GOR, hypersensitive oesophagus (no pathological reflux but positive correlation with reflux symptoms), or functional heartburn (no pathological reflux, no reflux-symptom association). Patients who were on proton pump inhibitors were excluded. Hypermobility questionnaire data from a group of 250 healthy volunteers was obtained from another study (3).

**Results:** 899 patients with complete data were included. HM was present in 18% of healthy controls. The prevalence of HM and the demographic characteristics of the patients in each reflux category is shown in Table 1. HM prevalence was highest in patients diagnosed with hypersensitive oesophagus (35%), and this was increased compared to HM prevalence in pathological GOR (22%, $p = 0.003$), functional heartburn (14%, $p < 0.0001$) and healthy controls (18%, $p = 0.0002$). HM prevalence in pathological GOR and functional heartburn was not significantly different to that in controls ($p = 0.2$ for both). Even after adjustment for age and gender, HM prevalence in hypersensitive oesophagus was significantly increased compared to that in other reflux diagnoses (17%): ORadj 2.06, CI:1.3–3.3, $p = 0.003$.

**Table 1:** HM prevalence and demographics in each reflux category

| | Pathological GOR n = 367 | Hypersensitive oesophagus n = 133 | Functional heartburn n = 399 |
|---|---|---|---|
| Females n, (%) | 187 (51%) | 88 (66%) | 254 (64%) |
| Median age (IQR) | 50 (38–60) | 43 (31–53) | 49 (38–59) |
| HM prevalence n, (%) | 81 (22%) | 47 (35%) | 55 (14%) |

**Conclusion:** The prevalence of HM in patients with hypersensitive oesophagus was almost twice as high as in healthy controls, whereas the prevalence in other phenotypes of reflux disease (pathological GOR and functional heartburn) was not significantly different to controls. This suggests that HM is over-represented in and associated with oesophageal hypersensitivity. Hypermobile patients may represent a distinct subgroup within the hypersensitive oesophagus category.

**Disclosure of Interest:** A. Fikree: I am part of the working group for the gastroenterology section of Ehlers-Danlos Syndrome-International
Q. Aziz: Prof Aziz is part of the working group for the gastroenterology section of Ehlers-Danlos Syndrome-International
All other authors have declared no conflicts of interest.

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## P1002 THE PREVALENCE OF GERD IN PRIMARY CARE PATIENTS IN RUSSIA: PRELIMINARY DATA OF THE MULTICENTER STUDY

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**Introduction:** Population-based MEGRE study (7812 subjects in 6 cities of Russia) performed in 2005–2006 showed that the average prevalence of GERD (Mayo Clinic Questionnaire) proved to be 13.3%.

**Aims & Methods:** The aims of the multicenter study are to determine the current prevalence, clinical spectrum of GERD and usage of medications for GERD treatment among in the urban population of Russia. Self-completion study questionnaire was performed on randomly selected 1734 patients of primary health care in the cities of Russia (Moscow, Kazan, Tver, Ryazan): 1059 females, 675 males, average age $46.1 \pm 14.4$ years. The questionnaire assessed the frequency, intensity of heartburn and regurgitation, medications consumption and frequency of their administration. Major symptoms (heartburn and/or regurgitation) were defined as "frequent symptoms" when occurring at least once a week or more. Patients were defined as having GERD if they reported frequent heartburn and/or regurgitation.

**Results:** Frequent heartburn was reported by 459 (26.5%), frequent regurgitation - by 281 (16.2%) of respondents. Prevalence of GERD among primary care patients was 30.8%. Importantly, we found that only 71.7% of subjects with GERD had seen a physician for this symptom. No difference was found in prevalence of frequent heartburn and/or regurgitation among women and men. Respondents with GERD took following medications for the last year to relieve the symptoms: PPIs −47.6%, $H_2$-blockers −20.4%, antacids −82.8%, alginates −24.2%, prokinetics −16.5%. Patients took the drugs at least once a week or more: PPIs −40.8%, $H_2$-blockers −15%, antacids −66.7%, alginates −17.8%, prokinetics −12.5%. PPIs were recommended by physician in 81.6% of cases, $H_2$-blockers – in 83.5%, antacids −65.2%, alginates −69%, prokinetics −82.8%.

**Conclusion:** Preliminary results of this study indicate a high prevalence of GERD among primary care patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1003 QUALITATIVE EVALUATION OF THE COMPOSITION OF REFLUXATE BY 24-HOUR MULTICHANNEL ESOPHAGEAL INTRALUMINAL IMPEDANCE AND PH-MONITORING AND ITS RELATIONSHIP WITH EXTRAESOPHAGEAL REFLUX DISEASE

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**Introduction:** Gastroesophageal reflux disease (GERD) is a disease caused by backflow of gastric contents into the esophagus due to the failure of physiological antireflux mechanisms and can lead to esophageal and extraesophageal symptomatology. Extraesophageal reflux (EER) is a condition where refluxate penetrate above the upper esophageal sphincter (UES) in to the oral cavity, pharynx, upper and lower respiratory tract and leads to pathological changes like e.g. hoarseness, chronic cough, vocal fold granuloma, globus pharyngis, laryngitis, pharyngitis, rhinosinusitis, otitis media, laryngeal tumors, bronchial asthma, COPD, sleep apnea and noncardiac chest pain. GERD can cause these symptoms directly by aspiration or indirectly by neurally mediated vagal reflex.

**Aims & Methods:** The examinations were carried out using 24-hour multichannel intraluminal impedance and pH esophageal monitoring (MII-pH), which compared to the more commonly used conventional pH-monitoring can accurately detect reflux episodes at all pH levels and divide the episodes to acid reflux ($pH < 4$), weakly acidic reflux (pH 4–7) and nonacid reflux ($pH > 7$), and also provides information of the composition of refluxate (liquid, gas and mixture). We evaluated results of the examinations from 200 patients in two groups. The first group included 100 patients (56 female and 44 male, mean age 47.8 years (range 12–71 years) with GERD and typical esophageal symptomatology. In the second group were 100 patients (56 female, 44 male, mean age 45.8 years (range 16–72 years) with EER symptoms, 52 patients were sent for examination by ENT specialist, 31 patients were from pulmonary clinic, 16 patients were from allergology department and one patient was sent from cardiology clinic. We evaluated DeMeester score, the number of reflux episodes by pH (acid, weakly acid and non acid), simultaneously the state of matter (liquid, gas, mixed) and the rate of penetration in the UES area. Statistical data were evaluated using Mann-Whitney test, Fisher's exact test and Wilcoxon paired test.

**Results:** We found a statistically significant difference ($p < 0.001$) in the value of DeMeester score that were significantly lower in the group with EER (median 21.6 vs. 45 in the GERD group). Further, in the group with EER against the group with GERD we observed significantly less episodes of mixed acid reflux ($p < 0.05$) and total acid reflux ($p < 0.05$) and higher number of mixed weakly acid reflux episodes ($p < 0.01$) gaseous weakly acid reflux episodes ($p < 0.01$) and total weakly acid reflux episodes ($p < 0.01$) and increased total number of gaseous reflux episodes ($p < 0.05$). Furthermore, in the group with EER against the group with GERD we observed significantly higher number of liquid ($p < 0.05$), mixed ($p < 0.05$), gaseous ($p < 0.001$) and overall ($p < 0.01$) reflux episodes in the level of electrode Z1 (UES). Also, we observed an increased fraction of non acid reflux episodes in the group with EER (27% versus 15% of patients with GERD), but without statistical significance ($p = 0.055$). We also compared the components of the acid and weakly acid reflux within groups of patients with GERD and EER, where we have seen in the group with GERD statistically significantly more episodes of mixed acid reflux against mixed weakly acid reflux ($p < 0.001$) and lower values of gaseous component of acid reflux against the gaseous component of weakly acid reflux ($p < 0.001$). In the group with EER as in the group with GERD were fewer episodes of gaseous acid reflux against the gaseous weakly acid reflux ($p < 0.001$), but a larger total number of reflux episodes of weakly acid to acid reflux ($p < 0.001$).

**Conclusion:** Patients with EER symptoms have more weakly acid reflux episodes and fewer acid reflux episodes compared to a group of patients with classical GERD symptoms while we found minor differences in the frequency of individual components of refluxate. We also observed lower values of DeMeester score, a higher number of gaseous reflux episodes and generally significantly higher number of penetration of refluxate of all states of matter to the UES area. These differences can suggest different pathophysiological mechanism of

symptoms of EER and GERD and also the necessity of different therapeutic approach to both groups in the future.
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## P1004 STUDY OF THE PREVALENCE OF GERD SUBTYPES IN THE NATURAL POPULATION WITH HIGH ESOPHAGEAL CANCER INCIDENCE OF CHINA

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**Introduction:** There have been few studies on the prevalence of GERD subtypes in the natural population in China.
**Aims & Methods:** The aim of the research is to study the prevalence of reflux esophagitis (RE) and non-erosive reflux disease (NERD) in the natural population with high esophageal cancer incidence of China combined the questionnaire screening and endoscopy examine. A population-based, randomized, cross-sectional study was conducted by site investigation of residents between 20~70 years old in Hua County of the Henan province, an area with high esophageal cancer incidence. Those with self-reported history of cancer, cardiovascular disease, mental disorder, etc. were excluded. All the subjects underwent Gerd Q investigation, the blood test, gastro-endoscopy with routine lodine dye and esophageal biopsy. According to the Los Angeles classification, RE was classified into four grades: LA-A, LA-B, LA-C and LA-D. NERD was diagnosed if Gerd Q score≥8 without esophageal mucosal damage. The data was inputted in the database and analyzed.
**Results:** Total 3291 residents (56.61 ± 7.62yrs, M: F = 1624:1667) completed the protocol. There were 19 subjects were identified to suffered from esophageal cancer, 3 gastric cancer, 31 gastric ulcer, 24 duodenal ulcer and 1 complex ulcer. ① Total 15.80% (520/3291,58.35 ± 7.15yrs, M:F = 328:192, P < 0.001) subjects were considered GERD with positive Gerd Q screening or/and endoscopy examine. ②10.15% (334/3291) subjects (M:F = 177:157, P = 0.166) were found positive with Gerd Q scores ≥8. The Gerd Q positive rate were 1.96% (1/51) in subjects with age less than 40yrs, 6.89% (59/856) in 41~50yrs, 9.03% (108/1196) in 51~60yrs and 13.97% (166/1188) in 61~70yrs, respectively (p < 0.001). Among them, 90 were RE, so the rest of 7.41% (244/3291) were diagnosed as NERD (58.51 ± 7.21yrs, M:F = 110:134, P = 0.183). The prevalence rate of NERD were 1.96% (1/51) in subjects with age less than 40yrs, 5.26% (45/856) in 41~50yrs,7.02% (84/1196) in 51~60yrs and 9.60% (114/1188) in 61~70yrs. ③276 subjects (8.39%, M:F = 218:58, P < 0.001) were identified as RE. Among them, 3.92% (129/3291) were LA-A grade RE, 4.32% (142/3291) were LA-B, and 0.15% (5/3291) was LA-C. None LA-D was detected. The detective rate of RE were 6.54% (56/856) in subjects with age 41~50yrs, 7.53% (90/1196) in 51~60yrs and 11.28% (134/1188) in 60~70yrs (P < 0.001). In addition, among 276 RE, 67.39% (186/276) were negative with Gerd Q investigation, and 28.26% (78/276) met the definition of silent RE.
**Conclusion:** The prevalence of GERD was 15.80% in the natural population with high esophageal cancer incidence of China. The prevalence of male was higher than that of female. The detective rates of RE and NERD were 8.39% and 7.41%, respectively. The age was older, prevalence rate was higher for both RE and NERD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1005 LIFESTYLE FACTORS AND GASTRO-ESOPHAGEAL REFLUX DISEASE: A CASE-CONTROL STUDY IN ALBANIAN ADULTS

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**Introduction:** The prevalence of Gastro-Esophageal Reflux Disease (GERD) in a population-based sample of Albanian adults has been recently estimated at 12% (1), which is lower than in many western European countries. Furthermore, GERD different environmental and lifestyle factors may contribute to its pathophysiology.
**Aims & Methods:** The aim of our study was to assess the association of GERD with lifestyle factors among adult men and women in Albania, a south-east European country still in the process of transition. A case-control study was conducted in 2013–2014 including 248 consecutive patients diagnosed with GERD at the Endoscopy Unit of the Regional Hospital Durres (142 men and 106 women, mean age: 46.5 years), and 273 GERD-free population-based controls (169 men and 104, mean age: 46.4 years; 85.3% response). A structured questionnaire included information about socioeconomic characteristics, behavioral factors and symptoms. Multivariable-adjusted binary logistic regression was used to assess the independent associations of lifestyle factors with GERD.
**Results:** GERD was positively associated with smoking, alcohol intake and physical inactivity. A similar positive association was found with body mass index and waist-to-hip ratio. Upon adjustment for socioeconomic characteristics, behavioral factors and anthropometric indices we found a negative association between GERD and daily intake of fruits, vegetables, whole-grain bread, boiled foods and olive oil (OR = 0.10, 95% CI: 0.03–0.31, OR = 0.14; 95% CI: 0.05–0.45, OR = 0.08; 95% CI: 0.02–0.26, OR = 0.06, 95% CI: 0.01–0.30 and OR = 0.03; 95% CI: 0.01–0.20, p < 0.05, respectively). There was no relationship between GERD and daily intake of tea, coffee, meat and butter.
**Conclusion:** We obtained evidence on the lifestyle correlates of GERD in Albania and the understanding of these modifiable risk factors can help to design the prevention and treatment strategies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1006 PATHOLOGIC ACID REFLUX IS NOT A COMMON FINDING IN PATIENTS WITH SEVERE DENTAL EROSIONS

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**Introduction:** Previous studies have shown that dental erosions might be a common finding in patients with gastroesophageal reflux disease (GORD), some studies reporting numbers as high as 32.5% (Loffeld, *Digestion* 1996). However results are conflicting and studies regarding the prevalence of pathologic acid reflux in patients with severe dental erosions of unknown etiology are lacking.
**Aims & Methods:** We retrospectively reviewed all patients referred to our department for an ambulatory 24 h pH registration between 2007 and 2015. In all, 1063 pH registrations were performed and 54 of these were referred due to severe dental erosions of unknown etiology. pH registrations were performed by a transnasally placed catheter with the pH sensor placed 5 cm above the proximal border of the lower esophageal sphincter, position determined by use of oesophageal manometry. A pathologic pH registration was defined as total acid exposure (pH < 4) of more than 4% of the registration time. A symptom association probability (SAP) ≥95% was considered positive. Baseline demographic data and symptoms suggestive of GERD (chest pain, acid regurgitations or retrosternal discomfort) were registered, both as indicated by the dentist in the referral note and by the patient during the registration. The results obtained in the patient group were compared with a group of 24 healthy controls (Krarup 2013).
**Results:** We included 54 patients (34 males (63%)), median age 41 years (range 16–71). GORD symptoms were mentioned by the dentist in the referral note of four (8%) patients, and during the 24 h pH registration by 13 (24%) patients. In all, 8 patients (15%) had a pathologic pH registration, a positive SAP in the 13 patients with symptoms was found in 53%, and the diagnostic yield in all was 16.5% (patients with either positive SAP or pathologic pH registration). Of the four patients with GORD symptom identified by the referring dentist, one had a pathologic pH registration (25% vs 15% in the rest of the cohort p = 0.5), and only this patient also had a positive SAP. Patients who reported GORD symptoms during the registration were significantly more likely to have a pathologic pH registration, compared to those without symptoms, 38.5% vs .7.5% (p = 0.006). Comparing patients with controls, patients were significantly older (41 vs. 29.5 years, p = 0.002) but the gender distribution was similar (64% vs. 63% men, p = 0.8). There were no significant differences between patients and controls with regard to proportion of time with pH < 4 (2% (0–25%) (median (range)) vs 0.9% (0–9.1%); p = 0.21), or acid exposure time in recumbent and upright positions (upright 2% (0–30%) vs 1.2% (0–12.5%); p = 0.18, recumbent 0% (0–26%) vs 0% (0–8.2%); p = 0.7). However in patients with GORD symptoms there was a significant difference in pathologic pH registration compared with controls (38.5% vs 8.5% p = 0.025). Duration of pH < 4 was significantly lower in upright position (6% (1–30%) vs. 1.2% (0–12.5%); p = 0.006) but not significantly for total (2% (0–18%) vs. 0.9% (0–9.1%); p = 0.077) or recumbent position (1% (0–8%) vs. 0% (0–8.2%); p = 0.25). Patients without any GORD symptoms (41/54), had a pathologic pH registration to the same extent as in controls (7.5% vs 8.5% p = 0.88).
**Conclusion:** In patients referred for 24 h pH registration because of dental erosions, pathologic acid reflux is not more common than in healthy controls. A careful symptom analysis before referral could possibly better identify patients who would benefit of 24 h pH registration in order to identify acid reflux as a putative cause of their dental erosions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1007 EXPRESSION OF LNCRNA CCAT2 IN PLASMA AS POTENTIAL BIOMARKER FOR DIAGNOSIS OF ESOPHAGEAL SQUAMOUS CELL CARCINOMA


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**Introduction:** Recent studies suggested that lncRNAs are stably detectable in the plasma or serum of tumor patients. Consequently, they can be identified as biomarkers for cancer patients. Identification of these markers that can be routinely monitored to predict the disease onset of cancer patients and prognosis of cancer patients would increase their median survival. We tested whether CCAT2, which was reported to be highly expressed in tissues of esophageal squamous cell carcinoma (ESCC), could also be regarded as a potential stable biomarker in the serum of ESCC patients.
**Aims & Methods:** 10 lncRNAs, which previously found to be over-expressed in ESCC, were selected as candidates for subsequent circulating lncRNA assay. After validating in 20 pairs of tissues and plasma in training set, CCAT2 was finally selected for further analysis in another 100 patients and 100 controls. We also used ROC curve to identify the sensitivity and specificity of this test.
**Results:** Plasma level of CCAT2 was significantly higher in ESCC patients compared with controls ($p < 0.0001$). By receiver operating characteristic curve (ROC) analysis, the area under the ROC curve (AUC) was 0.837; $p < 0.0001$; sensitivity, 83.3%; specificity, 73.3%. Furthermore, CCAT2 expression distinguished early stage ESCC from controls with AUC of 0.782; sensitivity, 62.2%; specificity, 89.5%. Additionally, plasma levels of CCAT2 were significantly lower in postoperative patients than preoperative ones ($p = 0.001$).
**Conclusion:** In conclusion, plasma CCAT2 could be regarded as a potential biomarker for ESCC diagnosis, particularly for early tumor screening.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1008 INSULIN PROMOTES ESOPHAGEAL ADENOCARCINOMA DEVELOPMENT IN A NON-OBESE MURINE MODEL AFTER SURGICALLY-INDUCED CHRONIC REFLUX


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**Introduction:** Insulin resistance and hyperinsulinemia could have a role in the growing incidence of Esophageal Adenocarcinoma (EAC) and its precancerous lesion Barrett's Esophagus, related to gastro-duodenum-esophageal reflux disease. These metabolic alterations are strictly linked to central obesity. Obesity condition is characterized by chronic systemic inflammation, increased levels of insulin like growth factor 1 (IGF1), steroids and peptides, that are showed to increase the risk of cancer. Furthermore, Human Epidermal growth factor receptor 2 (HER2) signaling activation is known to have a pivotal role in EAC carcinogenesis. A relationship between insulin and HER2 signaling was already demonstrated for breast cancer and it could be hypothesized also in this context.
**Aims & Methods:** The aim of this study was to evaluate the role of hyperinsulinemia in EAC pathogenesis, in the absence of any other confounding factor associated with obesity. To this purpose, we used the transgenic MKR murine model characterized by marked hyperinsulinemia and severe insulin resistance. Importantly, mice are not obese. Mice underwent duodenum-esophageal anastomosis in order to induce chronic reflux. Serum levels of glucose, insulin, C-peptide, leptin and IL-6 were quantified by Luminex-X-Map Technology. IR/IGF1R metabolic and mitogen signal pathways were analyzed in esophageal tissue. HER2 expression was evaluated by immunohistochemistry. Insulin signal and HER2 expression were evaluated also in insulin-treated OE19 human esophageal adenocarcinoma cell line.
**Results:** 29 normo-insulinemic wild type and 29 hyperinsulinemic MKR mice were sacrificed 30 weeks after surgically-induced reflux. 75.9% of MKR mice developed EAC compared with 34.5% of wild type ($p = 0.002$). The higher insulin concentration in MKR mice compared to wild type was responsible for insulin signal increase in esophageal tissue: IR and IGF1R were respectively two-fold and six-fold increased in MKR compared to wild type mice. A moderate HER2 expression was found in wild type neoplastic tissue, while a strong expression was found in MKR neoplastic esophageal tissues. In vitro, in absence of any other growth factor, insulin was able to induce HER2 overexpression and activation.
**Conclusion:** Hyperinsulinemia seems to have a pivotal role in EAC cancerogenesis related to chronic reflux independently from obesity condition. The insulin pro-cancinogenic mechanism could be also mediated by HER2 activation that, as known, could promote cell proliferation and invasion, inhibition of apoptotic mechanisms that, finally, are responsible for tumor onset and development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1009 IMMUNONUTRION BEFORE ESOPHAGECTOMY: IMPACT ON IMMUNESURVEILLANCE MECHANISMS


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**Introduction:** Esophageal adenocarcinoma is the fastest rising upper gastrointestinal malignancies in Western world and its outcome remains poor. Immunonutrition has been reported to improve the immune status of perioperative cancer patients. No data are known about the impact of immunonutrition on the immune microenvironment of esophageal adenocarcinoma. Mucosal immunesurveillance mechanisms might play a role in local recurrence after esophagectomy.
**Aims & Methods:** This study aimed to assess whether immunonutrition enriched in arginine, EPA & DHA and nucleotides could impact the immune cells responses in the local immune microenvironment of esophageal adenocarcinoma patients. Mucosal samples from healthy esophagus were obtained from 17 patients in QOLEC trial who had oral immunonutrition (Impact(®), Nestlé) for 5 days before esophagectomy were compared to those obtained from 65 patients who had esophagectomy and no supplementation. Markers of activation of antigen presenting cells (CD80, CD86 expression), innate immunity (TLR4, MyD88 expression) and cytotoxic lymphocyte infiltration (CD8, CD38, CD69 and CD107) were measured with imunohistochemistry and RT-PCR. Non parametric statistics was carried on.
**Results:** In healthy esophageal mucosa in patients having oral immunonutrition CD80 mRNA levels tended to be higher compared to patients who had no supplementation ($p = 0.08$). Moreover, in patients who had immunonutrition TLR4 mRNA were significantly higher than in those who had no supplementation ($p = 0.009$). Finally, in patients having oral immunonutrition lymphocyte infiltration (CD8+) and degranulation (CD107+) were significantly increased ($p = 0.04$ and $p < 0.001$, respectively).
**Conclusion:** Immune modulating nutrition seems to activate all the main immune surveillance mechanisms [1] in healthy mucosa of patients having esophagectomy for cancer. These results suggest possible impact of immunonutrition on adenocarcinoma local recurrence after esophagectomy and encourage the design of adequately powered clinical trials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1010 EFFECT OF NEOADJUVANT THERAPY ON DYSPHAGIA IN ESOPHAGEAL CANCER PATIENTS- DATA FROM A RANDOMIZED CONTROLLED TRIAL COMPARING CHEMOTHERAPY TO CHEMORADIOTHERAPY

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**Introduction:** Dysphagia, often accompanied by significant weight loss, is the main symptom leading to the diagnosis of esophageal cancer (Lagergren and Lagergren, 2013). Due to the elasticity of the esophageal wall, esophageal cancer usually gives no symptoms until the tumor obstructs the larger part of the lumen, and often the disease has then already reached an advanced stage (Rubenstein and Shaheen, 2015). A currently common clinical problem is how to manage dysphagia and secure nutrition during neoadjuvant treatment. In a recent pilot study from our group we showed that dysphagia in esophageal and junctional cancer decreased significantly already after the first cycle of platin based neoadjuvant chemotherapy, and decreased even more after completed nCT and nCRT (Sunde et al 2014). Though there is still a gap in knowledge regarding how nCT compared with nCRT affects dysphagia.
**Aims:** To investigate patient reported dysphagia before and after neoadjuvant treatment comparing neoadjuvant neoadjuvant chemotherapy (nCT) and neoadjuvant chemoradiotherapy (nCRT). Furthermore we aimed to explore the association between dysphagia relief and histological response on the two neoadjuvant therapy options.
**Methods:** A multicentre randomized controlled trial acronymed NeoRes comparing nCT with nCRT before surgery. Studypopulation was among 181 patients randomized in Sweden and Norway that answered dysphagia items using European Organisation for Research and Treatment of Cancer (EORTC)- esophageal specific instrument QLQ OES24/OG25 (n = 152). Histologic response was reported according to Chirieac Tumor Regression Grade.
**Statistics:** Data were analysed according to the EORTC manual. SAS proc mixed model was constructed to analyse repeated data with dysphagia effect and dysphagia-treatment adjusted with gender, age and histologic response. The distribution of characteristics between the two group treatment groups (nCRT and nCT) was described and compared, using Chi-square and Mann-Whitney U test where appropriate.
**Results:** Among 91 patients answering both dysphagia questionnaire before and after neoadjuvant treatment (patients with stent excluded) we found that in nCT a mean dysphagia score was before treatment 41(32–51) and decreased to 25(12–39) after neoadjuvant treatment, with a mean score difference on −16 and a p-value = 0.018. In nCRT arm mean score before neoadjuvant treatment was 41(30–50) and decreased to 28(17–39) after neoadjuvant treatment with a mean score difference −13 with a p-value = 0.081. In comparison between the arms nCT versus nCRT no score difference was detected between the groups (difference = 3). In both arms a statistical significant reduction was seen in problem to eat solid food. In nCT we detected a decrease from mean 60 before treatment to mean 31 after neoadjuvant treatment (p = 0.002) and nCRT mean 58 before treatment to 36 after neoadjuvant treatment (p = 0.005). Among patients without dysphagia we detected in nCRT arm a statistical significant increase of dysphagia (p = 0.006) after neoadjuvant treatment but stable among patients with nCT (p = 0.15). In comparsion between the arms nCT versus nCRT the increased dysphagia after neoadjuvant treatment in cohort without dysphagia had mean difference of 14 and a p-value = 0.008. In the other comparsions no difference were detected between the arms. We detected no association between dysphagia response and histologic response (p = 0.473).
**Conclusion:** Dysphagia improved after nCT, while not statistically significant after nCRT. In both arms a statistically significant ability to eat solid food was detected. In nCRT arm we detected a statistical significant increase of dysphagia. No correlation between change of dysphagia score and histologic response was detected using generalized linear mixed effect model.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1011 THE CLINICAL AND SERVICE IMPACT OF THE NATIONAL OESOPHAGO-GASTRIC CANCER AWARENESS CAMPAIGN: A LOCALITY ANALYSIS FROM COUNTY DURHAM

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**Introduction:** The UK national 'Be clear on cancer (BCOC)' campaigns led by Public Health England aim to improve public awareness of symptoms of cancer with a view to make an early diagnosis and reduce deaths arising from advanced disease. The 2015 national campaign for oesophago-gastric (OG) cancer ran from 26 January to 22 February with a key message of 'Having heartburn, most days, for 3 weeks or more could be a sign of cancer – tell your doctor' and a secondary message of 'Food sticking when you swallow could be a sign of cancer – tell your doctor.' The initial analysis of endoscopic outcomes of the national campaign suggested no significant increase in diagnosis of OG cancers. A locality impact analysis has not been reported so far.
**Aims & Methods:** This study is aimed as an impact analysis of the BCOC Oesophago-gastric cancer campaign in a specific locality of South Durham Hospitals (Darlington Memorial and Bishop Auckland[DA(CG1]). It aims to assess two aspects of the campaign: (1) clinical gain of a diagnosis of OG cancer and (2) the service impact of the increase in endoscopy demand as 2WW and routine referrals. Methods: Upper GI endoscopic data was captured from an electronic Endoscopy Scheduling software, as additions to gastroscopy waiting lists at two periods of time: 4 weeks after the OG campaign, in March 2015 and 4 months after the campaign, in July 2015. These included referrals from general practitioners for upper gastrointestinal symptoms in February/March 2015 (to coincide with the campaign period) and June/July 2015 (to coincide with a non-campaign period). Referrals for variceal screening, Barrett's surveillance, inpatient referrals or patients already known to secondary care were excluded. Of 760 cases, 407 were selected.
**Results:** There were a total of 284 referrals (2WW-149, urgent[DA(CG1] −66, routine-69) during the campaign period, which was 2.2 times greater than non-campaign period of 123 referrals (2ww-79, urgent-9, routine-35). The age distribution of cases was similar during both periods, with patients aged 61–80 having highest referral rates. Gender distribution was fairly similar across both periods for 2ww and routine referrals. However, there were 2.4 times more females referred urgently during the campaign period compared to male patients. During the campaign, despite an increase in referrals, there was no significant incease in OG cancer diagnosis. Only 2 OG cancers (1 oesophageal squamous cell carcinoma, 1 gastric adenocarcinoma) were diagnosed from 2ww referrals, while none was diagnosed from urgent or routine referrals. These 2 patients presented with dysphagia and weight loss. During the non-campaign period however, 3 malignancies were detected from 2ww referrals. Only one was an OG cancer (gastric adenocarcinoma), the other two had normal gastroscopies with malignancy detected on imaging (lymphoma, metastatic adenocarcinoma of unknown origin). There was no impact on average waiting time from referral to endoscopy for urgent referrals during both periods (29–42 days). The main impact on waiting times was seen for routine referrals: an increase from 29–42 days during non-campaign period to 43–56 days during the campaign period.
**Conclusion:** A national Oesophago-gastric cancer awareness campaign produces a significant increase in the number of referrals for gastroscopy, which has an impact on routine waiting times. The campaign has not shown any increase in diagnosis of OG cancers, thereby indicating that other strategies need to be considered for reducing deaths due to these cancers.
**Disclosure of Interest:** A. Dhar: Consultant for: Abbvie, Takeda
All other authors have declared no conflicts of interest.

## P1012 ESOPHAGEAL STRICTURES AFTER CHEMORADIOTHERAPY FOR ESOPHAGEAL CANCER; PREDICTORS AND SURVIVAL RATE

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**Introduction:** Chemoradiotherapy (CRT) has been an important role in the treatment of inoperable esophageal cancer. Esophageal strictures sometimes occur after CRT, which cause patients dysphagia. Although there are several studies about esophageal strictures, their clinical courses are unknown.
**Aims & Methods:** The aim of this study was to clarify the predictors for esophageal strictures and examine survival rate. This study was a retrospective and single-center study. Sixty patients with esophageal cancer received CRT between April 2011 to October 2013. We clarified predictors of the esophageal strictures after CRT by comparing the patients with stricture and those without it, and examined a 3-year survival rate. Strictures were defined as the condition that the endoscope (9.8 mm in diameter) did not pass thorough. This study was approved by the institutional review board of our hospital.
**Results:** Esophageal strictures occurred in 16 of 60 patients (27%). In the univariate analysis, longitudinal diameter (7.2 ± 0.5 cm vs 5.0 ± 0.3 cm), the proportion of tumor to the whole esophageal lumen (3/4< / <3/4:p = 0.006), and tumor depth (T3-T4 / T1-T2:p = 0.002) were significant predictors of esophageal strictures. The multivariate analysis revealed that longitudinal diameter of ≧7.0 cm (OR, 6.11; 95CI, 1.50−29.11) and tumor depth of T3-T4 (OR, 6.15; 95CI, 1.42−35.69) were significant predictors. The 3-year survival rate of the patients with strictures was 31% and that without strictures was 67%. The

survival rate of the patients with esophageal stricture was significantly lower than the rate without stricture (p=0.002).
**Conclusion:** Longitudinal diameter of 7.0 cm and tumor depth of T3-T4 were significant predictors for esophageal strictures after CRT. The survival rate of the patients with esophageal strictures was significantly lower than the rate without strictures.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1013 CLINICAL EFFICACY OF POLYGLYCOLIC ACID SHEET TO PREVENT ESOPHAGEAL STRICTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Stricture after endoscopic submucosal dissection (ESD) for superficial esophageal neoplasm with a mucosal defect involving more than three-quarters of the circumference is frequent. This prospective cohort study examined the clinical efficacy of application of polyglycolic acid (PGA) sheet with fibrin glue for the prevention of esophageal stricture after ESD.
**Aims & Methods:** We conducted a prospective study on eight patients with superficial esophageal neoplasm treated by ESD, who had a more than three-quarter including whole circumferential defect. After resection, PGA sheets were placed over the mucosal defect. Endoscopy was performed 2 days, 4 weeks, and 8 weeks after ESD, and esophagogram was performed 8 weeks for evaluating the degree of stenosis. In addition, dysphagia scoring scale at 8 weeks was investigated. Results were compared with a historical control group of nine patients who underwent ESD without PGA. The primary endpoint was the post-ESD stricture rate. Secondary endpoints included dysphagia score, degree of stenosis, the number of endoscopic balloon dilation sessions, and the occurrence of adverse events.
**Results:** Compared with the historical control group, the study group had a significantly lower stricture rate (12.5%, 1/8 patients vs. 66.7%, 6/9 patients; $P = 0.024$). There was a lower 8-week dysphagia score in PGA group than control group ($0.63 \pm 1.41$ vs. $2.22 \pm 1.56$; $p = 0.044$). In addition, frequency of severe stenosis was 12.5% and 55.6% in PGA and control group, respectively ($p = 0.054$). Number of EBD sessions was lower in PGA group with borderline level of statistical significance ($0.25 \pm 0.70$ vs. $2.00 \pm 2.24$; $p = 0.052$). There was no serious adverse event in both groups.
**Conclusion:** PGA application showed favorable outcome for the prevention of stricture after ESD for superficial esophageal neoplasm.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1014 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA IN CERVICAL ESOPHAGUS

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**Introduction:** Since the cervical esophagus (CE) is the narrowest portion of the esophagus, it is difficult to observe endoscopically due to anatomical constriction and gag reflex. Therefore, most of the CE cancers were detected at advanced stage, and often required total laryngectomy to achieve cure. Although the clinical benefit of endoscopic resection (ER) for superficial cancer in the thoracic esophagus is clarified, little is known for lesions in the CE because of low detection rate in superficial cancer.
**Aims & Methods:** The aim of this study was to clarify the clinical outcomes of ER for superficial squamous cell carcinoma (SSCC) of the CE. We enrolled consecutive patients with SSCC lesions in the CE who underwent ER at the National Cancer Center Hospital East between January 2009 and June 2015. The indication criteria of ER was as follows; 1) invasion depth was limited within SM1, 2) absence of clinical lymph node or distant metastasis. The definition of the CE referred to UICC TNM Classification, 7th Edition. An esophageal stricture (ES) was defined that endoscope with ordinary diameter could not pass through and endoscopic balloon dilation was required due to stricture symptom. We retrospectively analyzed clinocopathological factors and clinical courses after ER for SSCC in the CE. This study was approved by the institutional review board in our institution.
**Results:** A total of 33 patients (29 male and 4 female; median age of 69 years; range 49–85) with 37 lesions were enrolled. In the past histories, thoracic esophageal cancer and head and neck cancer (HNC) were found in 21 (64%) and 16 (49%) patients, respectively. 8 patients had other synchronous cancers (7 HNCs and one gastric cancer). 20 lesions limited in the CE, and the remaining 17 lesions extended to the upper thoracic esophagus. Conventional endoscopic mucosal resection and endoscopic submucosal dissection were performed in 10 and 27 lesions, respectively. Of the 37 lesions, 35 (95%) were resected en bloc, and 19 lesions were treated with ER under general anesthesia. In addition, 7 patients underwent simultaneously ER for another superficial HNC. Serious complications involving perforation or bleeding required intervention or transfusion were not observed. Median size of lesion was 16 mm in diameter (range: 3–52), and depth of tumor invasion; EP/LPM/MM/SM1/SM2 were 20/9/4/0/4 lesions, respectively. The luminal circumferences of mucosal defects after ER; $<1/2$ / $\geqq 1/2$ and $<3/4$ / $\geqq 3/4$ were 15/11/11, respectively. While a total of 12 patients developed ES, all of them recovered with repeated balloon dilation. Of the 12 patients, 10 had 3/4 or larger mucosal defect after ER, with ES rate of 91%. At the median follow-up period of 23 (range: 4–68) months after ER, local recurrence was detected in one (3%) patient alone. Metachronously superficial thoracic esophageal cancer was detected in 9 (27%) patients, and superficial HNC was detected in 7 (21%). All lesions were detected with follow-up endoscopy, and all of them except for one were treated with ER or partial resection under organ preservation. No lymph node or distant metastasis was detected in all patients, and no patients required laryngectomy and died with primary esophageal cancer in the CE.
**Conclusion:** Conclusion: Clinical benefit of ER for SSCC in the CE could be clarified because of curative potential under organ preservation. Careful observation in follow-up endoscopy after ER would be very important not only for early diagnosis of local recurrence but also for early detection of metachronous thoracic esophageal cancer and HNC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1015 ENDOSCOPIC ULTRASOUND (EUS) FOR PSEUDOACHALASIA, HISTORY REVISITED!

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**Introduction:** Pseudoachalasia is an infrequent secondary form of achalasia which can result from malignant or benign tumours, postoperative complications or paraneoplastic syndromes. Management can be vastly different between achalasia and pseudoachalasia, making it important to exclude the latter condition. Oesophago-gastro-duodenoscopy (OGD), high resolution manometry (HRM), barium oesophagram, CT scan and EUS play complementary roles to procure a diagnosis of achalasia and exclude pseudoachalasia.
**Aims & Methods:** This is one of the few studies that aims to evaluate the role of EUS in excluding pseudoachalasia for patients referred for achalasia workup. Data was collected retrospectively from hospital electronic records from 2008 to 2015. Our study group comprised 77 patients (female = 44, male = 33) with a mean age of 62 years. All cases had a prior OGD and EUS performed. Only cases with a non-diagnostic OGD (including negative esophageal biopsies) were included. Cases with obvious mass seen on OGD were excluded. Work up included the following:(A) classic achalasia symptoms, (B) normal OGD, (C) positive HRM +/-barium for achalasia/gastro-oesophageal junction outflow obstruction (GOJ-OO) and (D) had CT scan performed. Yield of excluding pseudoachalasia with addition of EUS was analysed in 4 groups: (1) A+B, (2) A+B+C, (3) A+B+D and (4) A+B+C+D. Cases referred without information on manometry, barium or CT findings were excluded appropriately in the subgroup analysis. Surveillance was performed within 6–12 months to detect any missed cases of pseudoachalasia. Statistical analysis was performed using SPSS V20 using the McNemar Chi-Square and Cochran's Q.
**Conclusion:** In excluding pseudoachalasia, additon of EUS to a well complemented workup (typical symptoms, OGD, HRM and/or CT scan) may not yield statistically significant benefit. However, EUS demonstrated good sensitivity and excellent specificity, PPV and NPV for pseudoachalasia detection clinically and should be considered on a case-by-case basis especially in any diagnostic dilemma.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Table 1:** Additional Detection of Pseudoachalasia with EUS Modality A = classic achalasia symptoms B = normal EGD/oesophageal biopsies C = positive HRM +/-barium for achalasia/variant/GOJ-OO D = had CT scan performed NS = not significant *some cases were excluded in subgroups (2), (3) and (4) due to missing input as external referral centre did not provide detailed results of certain investigations in C and/or D Almost all patients (98.7%) had dysphagia as one of the main symptoms. OGD was non-diagnostic in all cases. EUS was performed in all patients. Number of pseudoachalasia cases detected in Group (1)[n = 77], Group (2)[n = 53], Group (3)[n = 38] and Group (4)[n = 26] were 0, 0, 3 and 0 respectively. With addition of EUS (Table 1), incremental detection of pseudoachalasia in these respective cohorts were 7.8% (p = 0.031), 1.9% (p = NS), 0% (p = NS) and 0% (p = NS). EUS showed a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 85.7%, 100%, 100% and 98.6%. There was only 1 case of pseudoachalasia that was not picked up which manifested 2 years later. Other modalities (B, C and D) complemented each other to give excellent values of sensitivity, specificity and NPV.

| CATEGORY | (1)A+B (n = 77) | (2)A+B+C (n = 53) | (3)A+B+D (n = 38) | (4)A+B+C+D (n = 26) |
|---|---|---|---|---|
| Pseudoachalasia detection (cases) | 0 | 0 | 3 | 0 |
| Additional detection with EUS (cases) | 6 | 1 | 3 | 0 |
| Additional detection with EUS (%) | 7.8% (p = 0.031) | 1.9% (p = NS) | 0% (p = NS) | 0% (p = NS) |

## P1016 EFFICACY OF MODIFIED ORAL STEROID ADMINISTRATION FOR PREVENTING ESOPHAGEAL STRICTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** It has become possible to resect the superficial esophageal cancer of whole circumferential extension in en bloc fashion by ESD along with advancement of the ESD technique. However postoperative stenosis is sure to be developed, a countermeasure has been desired. Steroid injection or oral steroid administration is performed for extensive resection of non-whole circumference, and its effectiveness has been reported. But countermeasures for the entire circumference resection are not sufficient.

**Aims & Methods:** The aim of this study was to clarify the efficacy of modified oral steroid therapy which has done in our hospital and to clarify the current situation and challenges. Consecutive 25 patients underwent ESD of the entire circumference for superficial esophageal cancer from April 2010 to April 2015. Three patients were excluded because of additional surgery after ESD. So 22 patients were included in this study. Until January 2013 oral steroid had been administered for total 8 weeks, which was scheduled that 30 mg steroid was administered for 2 weeks, 25 mg for 2 weeks, and then 20 mg. 15 mg, 10 mg, 5 mg for 1week as an original method. Modified method, which was scheduled that 30 mg steroid was administered for 3 weeks, and then steroid was reduced in each 5 mg in 3 weeks interval, has been conducted since February 2013. Eleven patients were administered in original method, and 11 patients were in modified method.

**Results:** Four lesions were located at the upper site of the esophagus, 13 were at the middle, 5 were at the lower. All cases except 3 cases were performed ESD under general anesthesia. Procedure time was 114 minutes in average. There was no adverse event including post ESD bleeding and perforation. In the original method, esophageal stricture, which scope cannot pass through and dilatation was needed, prophylactic dilatation was performed in 2 patients. The median number of dilatation was 25, and mean number was 19.4. In the modified method, esophageal stricture and followed by balloon dilatation was developed in 4 patients (36%). The median number of dilatation was 0, and mean number was 6.2. Pneumonia and oral herpes infection were observed in 2 and 1 patients respectively as an adverse event in the original method, Candida esophagitis and arthritis were observed in 7 and 1 patients respectively in the modified method.

**Conclusion:** It was conducted safely to resect entire circumference of the esophagus by ESD. The frequency of esophageal stricture was lower in the modified method compared with original method, the number of balloon dilatation in the modified method was statistically lower than that in the original method (p = 0.028). Prophylactic measures for adverse events of steroid such as pneumonia should be paid attention.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1017 TREATMENT STRATEGY FOR LATERAL SPREADING SUPERFICIAL ESOPHAGEAL CARCINOMA

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**Introduction:** Thanks to recent development in upper GI endoscopy have enabled us to find superficial esophageal squamous cell carcinoma (ESCC). High-resolution endoscopy and image-enhanced endoscopy techniques such as magnifying endoscopy with NBI system allow detailed observations of microvessels pattern in superficial esophageal carcinoma, and we can estimate the depth of tumor invasion. Our indication of endoscopic treatment such as ESD for superficial ESCC is that depth of tumor is EP (epithelial layer), LPM (proper mucosal layer) regardless of the size. Even if the depth of tumor is MM (muscularis mucosae layer) or SM1 (surface layer of submucosa), the tumor is indication of diagnostic ESD. We assess the pathological data after diagnostic ESD, evaluate the risk of lymph node metastasis and decide the additional treatment, such as surgery and chemoradiotherapy (CRT). Estimation of the tumor invasion of lateral spreading (size is over 5 cm) superficial ESCC is difficult because of the size of tumor and accuracies are relatively lower compared to small lesions. Thus diagnostic ESD is the one of the options of treatment even for lateral spreading (size is over 5 cm) ESCC. Some of the patients have to undergo additional treatment because tumor is invaded to submucosal layer or lymphvascular invasion. On the other hand, wide resection by ESD could cause the delay of additional treatment because of the treatment for esophageal stricture after ESD. Thus, treatment strategy for lateral spreading ESCC has to include additional treatment after ESD.

**Aims & Methods:** From January 2010 to December 2014, 49 cases of lateral spreading superficial ESCC were resected by surgery (n = 17) or ESD (n = 32) in our hospital. Diagnosis, treatment methods and outcomes are evaluated. Our indications for additional treatment (surgery or CRT) after ESD are the cases of is over pT1b (SM), and even if the depth of tumor is MM pathologically invasive type, poorly differentiated ESCC or angiolymphatic invasion is indication of additional treatment, because of the high risk of lymph node metastasis.

**Results:** In 49 cases of lateral spreading superficial ESCC, 32 cases were treated by ESD and 17 cases were treated by surgery. Average age in ESD group is 67.8 years old (50–85 years old). Average size of tumor treated by ESD is 59.4 mm (50–85 mm). The depth of tumor invasion is pT1a-EP in 3 cases, pT1a-LPM in 12 cases, pT1a-MM in 11 cases, pT1**b**-SM1 in 1 case and pT1b-SM massive in 3 cases. Accuracies of estimated the depth of tumor invasion by preoperative endoscopic diagnosis for EP/LPM and MM/SM1 are 76.5% and 53.3%, respectively. Four of 32 cases of ESD underwent additional therapy (3 for surgery and 1 for CRT), because three cases are pT1b-SM2 and one case in pT1a-MM and lymphvascular invasion. In one case of 3 cases underwent surgery has lymph-node metastasis. Rate of stricture after ESD is 20.0% for sub-circumference ESD and 77.8% for circumference ESD even though injection of steroid. Average time and duration for control of esophageal stricture by Baloon Bougie is 13.5 times (4–32 times) and 18 weeks (7–32 weeks). No cases died by recurrence after ESD. Average age in surgery group is 65.7 years old (51–78 years old). Average size of tumor treated by surgery is 76.5 mm (50–130 mm). Seven cases in 17 (41.2%) have lymph node metastasis. Rate of lymph node metastasis is 0% (0/2 cases) for pT1a-LPM, 42.9% (3/7 cases) for pT1a-MM, 100% (1/1 case) for pT1b-SM1 and 42.9% (3/7 cases) for pT1b-SM massive. One case died by recurrence after surgery and 48 cases were survived without any recurrences.

**Conclusion:** Most of strictures after sub-circumference ESD could be prevented by steroid injection. However control of strictures after circumference ESD is difficult and takes long time. Thus, diagnostic ESD should not be performed for circumferencial lesions of lateral spreading superficial ESCC for the patients who want to undergo CRT for additional treatment after ESD, and undergo CRT without diagnostic ESD. Diagnostic ESD for circumferencial lesions for the patients who want to undergo surgery for additional treatment is acceptable. Long survival could be obtained by ESD or surgery for the patients of lateral spreading ESCC by our treatment strategy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1018 THE CLINICOPATHOLOGIC FEATURES AND PROGNOSIS IN YOUNG GASTRIC CANCER PATIENTS ACCORDING TO HELICOBACTER PYLORI INFECTION

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**Introduction:** *Helicobacter pylori* (*H. pylori*) is a risk factor for gastric cancer. Gastric cancer is believed to be a disease of the elderly, and rarely occurs in young patients. The aim of this study was to analyze the clinicopathological and prognostic factors in young (aged < 40 years) gastric cancer patients according to *H. pylori* infection.
**Aims & Methods:** A total of 515 young (aged < 40 years) patients with gastric cancer from 2003 to 2015 were enrolled in this study. The clinicopathological features of the young gastric cancer patients with *H. pylori* infection were compared with those of the young gastric cancer patients without *H. pylori* infection. The overall survival was the main outcome measure. The survival curves were constructed using the Kaplan-Meier method, Univariate analysis was performed using the log-rank test, and multivariate analysis was performed using with Cox regression.
**Results:** Of the 515 patients, those with *H. pylori* infection were assigned to the HP group (n = 257), and those without *H. pylori* infection were assigned to the non-HP group (n = 258). Kaplan-Meier analysis showed that the prognosis of gastric cancer in young patients with *H. pylori* infection was poorer than that in young patients without *H. pylori* infection (log-rank test, p = 0.021). The 5-year survival rates were higher in the non-HP group than in the HP group (88.3% vs. 79.7%, $p < 0.05$). The relative risk of death in the HP group compared to that of the non-HP group, after correction for age and gender, was 2.62 (95%CI: 1.46–4.81; p = 0.02). In univariate and multivariate analysis, pathologic differentiation, stage and cell type were related to gastric cancer in young patients with *H. pylori* infection ($p < 0.05$).
**Conclusion:** In young gastric cancer patients with *H. pylori* infection, the prognosis was poorer than that of young gastric cancer patients without *H. pylori* infection. The 5-year survival rates were higher in the non-HP group than in the HP group (88.3% vs. 79.7%, $p < 0.05$). The relative risk of death in the HP group compared to that of the non-HP group, after correction for age and gender, was 2.62 (95%CI: 1.46–4.81; p = 0.02).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1019 LYMPH NODE METASTASIS RISK FOR HISTOLOGIC TYPE WITH POORLY COHESIVE COMPONENTS IN EGC CONFINED TO MUCOSA

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**Introduction:** Although early gastric cancer (EGC) confined to mucosal layer, the risk of lymph node (LN) metastasis may be different according to characteristics of tumor including histologic type. However, there is little information about the LN metastasis risk for histologic type with poorly cohesive components such as poorly cohesive carcinoma (PCC) and mixed adenocarcinoma (MAC).
**Aims & Methods:** Of 692 EGC patients who had undergone gastrectomy with LN dissection, 147 (21.2%) EGCs were confirmed as mucosal cancer with poorly cohesive components.
**Results:** 147 EGCs were classified as PCC group (n = 127, 86.4%) and MAC (n = 20, 13.6%) based on WHO classification. PCC group had LN metastasis in 8 (6.3%). LN metastasis was detected in 2 PCCs > 20 mm in size and without ulceration, 2 PCCs ≤ 20 mm in size and with ulceration, and 4 PCCs > 20 mm in size and with ulceration. In addition, lymphovascular (LV) invasion was found in 2 PCCs > 20 mm in size and with ulceration. However, there was no LN metastasis or LV invasion in lesions ≤20 mm in size and without ulceration. No LN metastasis or LV invasion was detected regardless of ulceration and tumor in MAC group.
**Conclusion:** The risk of LN metastasis is little for histologic type with poorly cohesive components in EGC with mucosal invasion, less than 20 mm in size, and no ulceration. Considering tumor size, depth invasion, and the presence of ulceration in EGC, ESD can be treatment modality even in PCC or MAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1020 EPIDEMIOLOGY AND CLINICAL MANAGEMENT OF PATIENTS WITH GASTRIC MALT LYMPHOMA: THE FIRST POPULATION-BASED STUDY IN FRANCE

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**Introduction:** Gastric marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue (GML) is a rare disease whose clinical management has not been well standardized until recently. Our aim was to describe the principal epidemiological and clinical characteristics of GML in the general, non selected, French population.
**Aims & Methods:** All new cases of GML diagnosed between 2002 and 2010 in 11 French areas covered by registries were included. Pathology reports were verified and if necessary reviewed by an expert pathologist. Data were collected retrospectively from medical files. Age adjusted incidence rate was calculated and survival estimated using Kaplan- Meier method.
**Results:** Among 423 eligible cases, 7 (1.7%) were excluded after verification because of false diagnosis. Incidence rate of GML was 0.40 per 100,000 person-years (IC95% [0.36–0.44]). Among 416 patients with confirmed GML, 50.2% were males, with median age of 67 years (range 24–97) and 40 (9%) had a personal history of cancer. The median number of biopsies at diagnosis was 6 (range 1–20), and histological analysis by a referent pathologist was made in 56% of patients. Staging was performed in 340 patients, by CT-Scan (93%), endoscopic ultrasound (45%), or bone marrow biopsy (62%). Disease stage was indicated for 338 patients: 76% were at loco-regional- and 24% at advanced stage. *H. pylori* was searched in 393 patients (94%), and 57% of them were *H. pylori* (+) at diagnosis. Treatments were analysed in 339 out of 416 patients: 33 had no treatment and 44 cases were excluded because of histological transformation into high-grade lymphoma observed early after diagnosis putting in doubt initial histological typing as small cell GML. Out of 339 patients, 200 were *H. pylori* (+) and 193 of them (94%) received at least 1 line of eradication treatment. 190 patients received at least one other treatment (143 chemotherapy +/- immunotherapy, 25 radiotherapy and 5 surgery). A complete remission was obtained in 238 patients (70%). The 5-year overall survival was 82% (IC95% [77–85]), and was significantly higher in *H. pylori* (+) (87%)(IC95% [82–91]) than in *H. pylori* (-)(75%) %)(IC95% [67–81]) patients.
**Conclusion:** In the general population, the diagnosis of GML is sometimes difficult, with a risk of underestimating the degree of malignity, and is made at more advanced stages as compared to the patients included in clinical studies. The prognosis is better for *H. pylori* (+) than *H. pylori* (-) patients. This study underlines the importance of following the recent European guidelines in the clinical management of GML.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1021 DELICATE FEATURES AND SUBTLE DETAILS FOR CHARACTERIZATION OF GASTRIC EPITHELIAL NEOPLASIAS BY HIGH DEFINITION AND MAGNIFIED NARROW-BAND ENDOSCOPY

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**Introduction:** Magnified narrow-band imaging (ME-NBI) endoscopy is effective for differentiation benign and neoplastic gastric lesions. VS-classification (by K. Yao et al., Japan) is the most effective and widespread for this reason, but it is not easy to determine irregularity of microsurface and microvascular pattern.
**Aims & Methods:** Aim: to define the most important and easy high-definition narrow-band imaging (HD-NBI) and ME-NBI endoscopic features of the surface (pits) and vessels of gastric mucosa for differentiation benign and neoplastic gastric lesions. Materials and methods: We prospectively selected and described 220 HD-NBI (n = 175) and ME-NBI (n = 45) quality endoscopic images by 4 clinical (age, gender, etc.), 14 macroendoscopic (localization, size, microtype, etc.) and 16 microendoscopic parameters of microsurface and microvascular pattern. 220 images included 141 photos of benign lesions (hyperplastic polyps, erosions, ulcers, focuses of intestinal metaplasia) and 79 photos of neoplasia (low

and high grade IEN, EGC Tm, Tsm, GC Tmp). We compared benign and neoplastic lesions by 34 parameters with Fisher's exact test and Cramer's conjugation coefficient.
**Results:** We determined 17 statistically significant endoscopic parameters for differentiation benign and neoplastic lesions with accuracy 95% (94 and 97% respectively) by inhomogeneous Bayes sequential diagnostic procedure. Then we selected 6 the most significant, easy and objective endoscopic signs and we got differentiation benign and neoplastic lesions with accuracy 94% (92 and 96% respectively). The features of benign lesions: thickness of vessels in the lesion is even and more/same to surrounding mucosa, smooth edges of vessels, the ratio of pit and vessels thickness $P \leq V$, there are not demarcation line and bright dark vessels in the lesions by NBI visualization. The features of neoplastic lesions: thickness of vessels in the lesion is uneven and less to surrounding mucosa, uneven edges of vessels, the ratio of pit and vessels thickness $P > V$, there are demarcation line and bright dark vessels in the lesions by NBI visualization. We checked these 6 microendoscopic features for differentiation 40 endoscopic images (21 benign, 19 neoplastic) by 3 experts (accuracy 100%), 2 doctors with small experience (accuracy 92–95%, interobserver agreement (IA) $k = 0.75$) and 2 doctors without experience in HD-NBI endoscopy (accuracy 95–98%, IA $k = 0.85$). We also used computer analysis of endoscopic images to differentiate irregular vascular pattern in expert opinion and so determined the neoplasia with accuracy 85%.
**Conclusion:** In accordance with the analysis six microendoscopic features of gastric lesions were proven most significant for effective differential diagnosis between benign and neoplastic epithelial gastric lesions. These features can be successfully used by nonexperience doctors and also for creating the decision support system, including through the computer analysis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1022 TREATMENT STRATEGY OF ENDOSCOPIC RESECTION FOR SYNCHRONOUS DOUBLE EARLY GASTRIC CANCER: SIMULTANEOUS RESECTION VS. TWO-STAGE RESECTION

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**Introduction:** With the recent advances in endoscopic examinations, the number of patients with synchronous early gastric cancers (EGCs) fulfilling the indications for endoscopic resection (ER) has increased. There are several treatment strategies of ER for synchronous double EGCs, such as simultaneous ER carried out in the same session and two-stage ER carried out on separate days; however, the optimal treatment strategy has not yet been clarified [1].
**Aims & Methods:** The aim of this study was to clarify the optimal treatment strategy of ER for synchronous double EGCs by comparing the clinical outcomes of simultaneous ER and two-stage ER. A total of 1,398 patients with 1,690 EGCs in the normal stomach underwent ER (endoscopic submucosal dissection (ESD)/endoscopic mucosal resection (EMR) = 1,681/9) at our hospital from 2010 to 2014. Among 156 patients with 342 synchronous multiple EGCs, there were 133 patients with 266 synchronous double EGCs. In this study, 87 patients with 174 synchronous double EGCs treated by simultaneous ER in the same session (simultaneous ER group; 87 sessions with 174 resections [ESD/EMR = 169/5]) and 20 patients with 40 synchronous double EGCs treated by two-stage ER on separate days (two-stage ER group; 40 sessions with 40 resections [ESD/EMR = 40/0]) were included after excluding 26 patients with 52 adjacent, synchronous double EGCs in whom both the lesions were resected as one piece simultaneously. We retrospectively compared the clinicopathological findings and technical outcomes between the simultaneous ER group and the two-stage ER group. Synchronous double EGCs were defined as the double EGCs diagnosed at the same time.
**Results:** The clinicopathological findings in the simultaneous ER group vs. two-stage ER group were as follows; mean age (yr): $72.1 \pm 7.2$ vs. $72.3 \pm 8.8$ (NS [Not significant]); gender: male/female = 73/14 vs. 17/3 (NS); ASA physical status classification: class 1 or 2/class 3 = 71/16 vs. 14/6 (NS); mean tumor size (mm): $13.3 \pm 9.6$ vs. $20.5 \pm 12.3$ ($P < 0.0001$); present of ulceration: 2.3% (4) vs. 15% (6) ($P = 0.0026$); proportion of cases with lesions in the lower-third of the stomach: 44.3% (77) vs. 25% (10) ($P = 0.0254$). The technical outcomes were as follows; mean specimen size (mm): $34.6 \pm 11.9$ vs. $43.7 \pm 12.1$ ($P < 0.0001$); mean procedure time per resection (min): $55.7 \pm 41.3$ vs. $99.7 \pm 60.1$ ($P < 0.0001$); mean procedure time per session (min): $111.1 \pm 54.2$ vs. $99.7 \pm 60.1$ (NS); en-bloc resection: 99.4% (173) vs. 100% (40) (NS); R0 resection: 97.7% (170) vs. 95% (38) (NS); delayed bleeding per resection: 2.3% (4) vs. 7.5% (3) (NS); delayed bleeding per session: 4.6% (4) vs. 7.5% (3) (NS); perforation per resection: 2.3% (4) vs. 2.5% (1) (NS); perforation per session: 4.6% (4) vs. 2.5% (1) (NS); delayed bleeding and/or perforation per resection: 4.6% (8) vs. 10% (4) (NS); delayed bleeding and/or perforation per session: 8.0% (7) vs. 10% (4) (NS). All complications were managed conservatively.
**Conclusion:** Simultaneous ER appears to be preferable especially for synchronous double EGCs that are technically easy to resect, such as lesions that are non-ulcerative, small and located in the lower-third of the stomach, because of the favorable technical outcomes [2].
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1023 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR NON-AMPULLA DUODENAL NEOPLASIA

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**Introduction:** Duodenum is one the most difficult area for safe ESD, because of poor maneuverability, narrow space and thin proper muscle layer. Furthermore, the incidence of delayed complications including perforation and bleeding have been reported higher than that of gastric or esophageal ESD.
**Aims & Methods:** The aim of this study is to clarify the result of duodenal EMR/ESD, and the effect of suture for ESD ulcer to prevent delayed complications. Patient and method: A consecutive 111 duodenal neoplastic lesions treated by EMR/ESD from May 2001 to June 2015 were enrolled to this retrospective study. Male and Female were 84 and 31, respectively. Mean age was 60 (37–86). Bulbs, second and third portion were 8, 93 and 10, respectively. Adenocarcinoma and adenoma were 88 and 23, respectively. 0-I, 0-IIa and 0-IIc were 1, 59 and 51, respectively. Size of tumor and resected specimens were 9 (2–70) and 6 (8–58) mm, respectively. EMR, hybrid ESD (Mucosal incision, submucosal dissection + snaring) and ESD were performed for 19, 89 and 7 patients, respectively. Eight cases were followed up without closure (open group), and remaining 103 patients were followed up after closure of EMR/ESD ulcer by clip, endo-loop or laparoscopic assist (closed group).
**Results:** 1. Perforation during procedure: the number of perforation during EMR, hybrid ESD and ESD were 0, 1 (1/89) and 0%. The only perforated case was treated by clipping without surgery. 2. En-bloc resection rate of EMR, hybrid ESD and ESD were 75% (12/16), 93% (82/88) and 100% (7/7), respectively. 3. R0 resection rate were 69% (11/16), 84% (75/88) and 100% (7/7), respectively. R0 is defined as En-block resection, horizontal and vertical margin were negative. Therefore, piecemeal resected cases were judged as R1. The result of ESD and hybrid ESD is better than EMR. 4. Local recurrence rate were 19% (3/16), 0 and 0%, respectively. 5. 96 of 103 cases in closed group could be closed completely by clips. The average number of clips was 7.7. And remaining seven patients were treated combination by clip and ENPD/ENPD, laparoscopic closure and/or covering technique by Neoveil. 6. Delayed bleeding rate of closed and open groups were 2.8% (3/103) and 50% (4/8), respectively ($p < 0.0001$). All of three cases those tumor size was 21 mm or bigger in open group caused delayed bleeding. 7. Delayed perforation rate of closed and open groups was 0% and 13% (1/8), respectively ($p = 0.0012$).
**Conclusion:** Closure of EMR/ESD ulcer is effective to prevent delayed bleeding and perforation after duodenal EMR/ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1024 DKK-2, A MODULATOR OF WNT-SIGNALING PATHWAY, IS OVEREXPRESSED IN GASTRIC CANCER

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**Introduction:** Gastric cancer (GC) still ranks as one of the most common malignancies worldwide with high morbidity and mortality. The dickkopf gene family comprises four secreted proteins (DKK1–4), which modulate the Wnt-signaling pathway that plays a major role in gastrointestinal carcinogenesis. DKK-2 acts either as an activator or inhibitor of this pathway, but its role in gastric cancer is uncertain.
**Aims & Methods:** To evaluate the gene expression of DKK-2 in GC and normal gastric mucosa. Biopsies from a prospective cohort of 56 patients with gastric cancer (32 intestinal type, 24 diffuse type) and 20 non-cancer controls were analysed for DKK-2 and ß-catenin gene expression. From cancer patients, biopsies from tumour, adjacent normal and tumour-distant mucosa were retrieved, while antrum and corpus biopsies were obtained from healthy volunteers. DKK-2 transcript levels were quantified by realtime RT-PCR and protein expression was analyzed using immunohistochemistry (IHC).
**Results:** DKK-2 was expressed in 33.4% (diffuse type) and 40.7% (intestinal type) of GC samples, while no expression was seen in non-cancer controls. Gene expression was most increased in tumour compared to tumour-adjacent, and tumour-distant mucosa ($P < 0.001$). DKK-2-transcript levels were 88- and 6-fold increased in GC of the intestinal and diffuse type, respectively compared to the adjacent tumour-free mucosa ($P = 0.001$). The expression levels of DKK-2 and ß-catenin correlated significantly in tumor specimens ($r = 0.431$; $p = 0.002$). IHC confirmed protein expression of DKK-2 in 58.9% of the GC-samples ($P = 0.113$).
**Conclusion:** DKK-2 expression in GC is upregulated in tumour samples compared to adjacent normal and tumour-distant mucosa. This implies a functional role of DKK-2 in the Wnt-signaling pathway of gastric carcinogenesis. This

seems to account especially for the intestinal type of GC. Whether it may play a role in the clinical setting (i.e. clinical translation) should be further investigated.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1025 LOW-PASS FILTER VISUALIZES MARGINAL CRYPT EPITHELIUM OF GASTRIC MUCOSA WITH HIGH SENSITIVITY IN MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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**Introduction:** White zone visualized by magnifying endoscopy with narrow-band imaging (M-NBI) corresponds to stratified alignments of the gastric marginal crypt epithelium. White zone is, however, not necessarily traced even under the presence of crypt alignments. We have noticed that white zone has been effectively visualized by using low-pass filter even in cases with poor visual discrimination.
**Aims & Methods:** The aims of this study are to present an image processing method or low-pass filter for white zone and to compare detection sensitivity for crypt alignments between the image processing and visual evaluation. Eleven specimens of endoscopic submucosal resection from 8 patients with gastric cancer were used. M-NBI was taken serially along the line of interest. The pictures were processed by low-pass filter for white zone area (%), and visually classified into the presence (WZ+) or absence of white zone (WZ-) by a single endoscopist. The formalin-fixed-specimen was sliced along the same line of interest. The histological pictures was processed for averaged epithelial area (μm×mm) at 1 mm intervals.
**Results:** A total of 123 intervals were analyzed. In cancer intervals, 36 intervals were visually classified as WZ- and 30 as WZ+. In background, 11 intervals were visually classified as WZ- and 46 as WZ+. In cancer, white zone area was significantly lower in WZ- ($28.4 \pm 10.7\%$) than in WZ+ ($32.9 \pm 4.6\%$, $p = 0.0126$). In background, white zone area did not significantly differ between WZ- ($30.5 \pm 6.3\%$) and WZ+ ($33.5 \pm 4.3\%$, $p = 0.2508$). When the presence or absence of crypt alignments are defined as averaged epithelial area $\geq 20$ or $< 20$, respectively, detection sensitivity for crypt alignments in visual evaluation was 50% in cancer and 81% in background, and that in the image processing method was 100% both in cancer and background.
**Conclusion:** Low-pass filter was found to detect crypt alignments with a higher sensitivity than visual evaluation, possibly allowing auto-detection of early gastric cancer through pattern classification of crypt alignments.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1026 ENDOSCOPY GUIDED DA VINCI® ROBOTIC GASTRIC SURGERY FOR EARLY GASTRIC CANCER

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**Introduction:** Endoscopic resection has been an optimal treatment for selected patients with early gastric cancer (EGC) based on advances in endoscopic instruments and techniques. This study aims to evaluate the result of endoscopy guided da Vinci® Robotic full-thickness gastric resection (ERFTGR) with sentinel lymph node basin dissection (SLND) under indocyanine green and infrared in cases of EGC with high risk of lymph node metastasis.
**Aims & Methods:** This was a prospective, pilot study at a single academic center. Of 70 patients with EGC, 12 met the following criteria: 1) differentiated mucosal/submucosal cancer with an ulcer, between 3 and 4 cm by endoscopic imaging; 2) undifferentiated mucosal/submucosal cancer without an ulcer, between 2 and 3 cm by endoscopic imaging; 3) patients who had undergone previous ESD whose pathological reports recommended an additional gastrectomy due to a risk for LNM. The main outcome measure was technical success.
**Results:** All cases were resected en bloc with negative surgical margins. Previous forceps biopsy results revealed that 7 cases were undifferentiated adenocarcinoma. Three of the 10 cases were suspected submucosal cancer by endoscopic and EUS findings. The other 2 cases that had undergone previous ESD whose pathological reports recommended an additional gastrectomy due to positive vertical margin. After ERFTGR with SLND, 2 patients were observed lymph node metastasis and were underwent standard gastrectomy. ERFTGR with SLND was conducted without perioperative adverse events.
**Conclusion:** ERFTGR with SLND could be a bridge between ESD and conventional gastrectomy with respect to preventing an extensive gastrectomy in patients with EGC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1027 PPI TEST FOR DIAGNOSIS OF BODY ATRHOPIC GASTRITIS: A PROPECTIVE STUDY

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**Introduction:** Pepsinogen 1 (PG1) is a non-invasive test for diagnosis of body chronic atrophic gastritis (with a negative predictive value of 98%) but the upper cut-off to make the diagnosis is controversial, as in Europe is claimed to be under 30 mcg/l, while in Japan is considered under 70 mcg/l. Furthermore there is a "gray zone ", of not clear interpretation, in which patients with PG1 values ranging between 30 and 50 mcg/l could show histologic finding of CAG.
In the literature it's claimed that PG1 are increasing after PPI administration, within one week from the start of the therapy.
**Aims & Methods:** To identify patients with body chronic atrophic gastritis (CAG) in a population group showing serological PG1 levels borderline (30–50 mcg/l) by means of a PPI –test. 42 patients (M: F = 19: 23, mean age: 54.7 years) with a common finding of PG1 < 60 mcg/l were divided into 5 groups according with the values of PG1: Group A (n = 6, PG1 < 30 mcg/l), Group B (n = 15, PG1 30–35 mcg/l), Group C (n = 14, PG1 35–39 mcg/l), Group D (n = 5, PG1 40–49 mcg/l), Group E (n ° 2, PG1 50–60 mcg/l). The determination of PG1 values was made by using a commercial kit (Biohit Oyj, Helsinki, Finland). In every patients a full dose of PPI (40 mg of esomeprazole, once a day before breakfast) was administered for seven days. At the end of PPI administration the PG1 determination was repeated. An increase of less than 10% of PG1 values after PPI test was considered POSITIVE test in confirming the diagnosis of body atrophic gastritis. All patients underwent on upper G.I. endoscopy with gastric biopsies for diagnosis of gastritis, according with OLGA staging.
**Results:** In Group A levels of PG1 resulted not increased in 6 patients out of 6, in Group B in 11 patients out of 15, in Group C in 5 out of 14, in Group D in 3 to 5 and in Group E all the subjects showed an increase >10% of PG1 values from baseline. The correspondence between serology and histology to assess diagnosis of body atrophic gastritis was as follows: Group A 6/6; Group B: 14/15; Group C 13/14; Group D: 5/5; Group E 2/2.
**Conclusion:** The diagnosis by serology of CAG is filling 100% with the histological diagnosis, when PG1 values are less than 30 mcg/l, while in the range between 30 and 50 mcg/l ("gray zone") the use of PPI test can allow us to identify the true subjects with CAG from normal people, by using the "PPI Test" as previously described.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1028 PROGNOSTIC PREDICTORS IN PRIMARY GASTRIC DIFFUSE LARGE B-CELL LYMPHOMA

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**Introduction:** Gastrointestinal tract is the most commonly involved site in extranodal lymphomas. Majority are primary gastric lymphomas and 50% of these are diffuse large B-cell non-Hodgkin's lymphoma (DLBCL).
**Aims & Methods:** Evaluation of overall survival and potential prognostic factors, in patients with primary gastric DLBCL. Retrospective analysis of patients with gastric DLBCL diagnosed in a tertiary center, during a 11 years period. Analyzed demographic data, immunohistochemical characteristics, *H. pylori* infection status (HP), biological markers, staging, therapeutic approach, prognosis and survival.
**Results:** Thirty-six patients were included, 52.8% (19/36) males, median age of 69 years. Most of gastric DLBCL (n = 30, 83.3%) weren't associated with MALT component. In 33 patients in whom it was possible to determine Lugano staging, 15 (45.5%) were in stages I/II and 18 (54.5%) in stages III/IV. Twenty-four of the 32 patients (75.0%) underwent chemotherapy (CT) and 8/32 (25.0%) underwent

surgery with or without chemotherapy associated. The mean follow-up time was 39 months (mín.0; máx.123). Most patients, 66.7% (18/27), achieved complete remission; 1/27 (3.7%) had partial remission and 8/27 (29.6%) had no response or had disease progression. The overall survival at 1, 2 and 5 years was 61.1%, 45.7% and 34.5%, respectively. The univariate analysis showed that elevated $\beta$2-microglobulin ($>3$ mg/ml) (HR: 3.53, $p=0.065$), low albumin ($\leq 3.5$ g/dL) (HR: 0.14, $p=0.002$) and a high (3, 4 and 5) International Prognostic Index (IPI) (HR: 4.03, $p=0.012$), are associated with worse survival. There was no significant association between gender, age at diagnosis, immunohistochemical phenotype, HP infection, LDH, hemoglobin, platelets, Lugano staging and treatment modality and survival.
**Conclusion:** In this population, the $\beta$2-microglobulin values, albumin, and IPI were prognostic predictors factors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1029 GASTROINTESTINAL STROMAL TUMORS: NATURAL HISTORY AND OUTCOMES IN THE IMATINIB ERA


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**Introduction:** Before the advent of imatinib, the gastrointestinal stromal tumors (GISTs) were associated with a disease free survival rate of disease of 50% at 5 years, but the actual natural history of the disease is understood.
**Aims & Methods:** Our objective was to characterize the natural history and outcomes of GISTs in the imatinib era. For that, we performed a retrospective evaluation of patients with GISTs diagnosed in a tertiary referral center between January 2000 and June 2015.
**Results:** We included 131 patients, 55% female, with a mean age of $64 \pm 14$ years, followed for a median of 30 months (IQR: 11–68). 64% of cases had gastric involvement. Most patients (57%) had symptoms at diagnosis, including gastrointestinal bleeding (38%). 20% of the diagnoses were accidental. At diagnosis 55% were in stage I and 16% in IV (TNM classification). 92% of the tumors were c-Kit positive. According to the NIH risk classification, 28% of the tumors were classified as high risk. The accuracy of cytology in patients who underwent endoscopic ultrasound (21%) was 54%. 95% of patients were operated (complete resection: 89%). Imatinib was initiated in 25% of patients, as adjuvant therapy in 69%. 75% reported adverse effects, and 16% developed resistance that was associated with the presence of lymph node involvement ($p=0.025$) and positive immunohistochemistry for DOG-1 ($p=0.017$). The recurrence rate was 4%, and was associated with age at diagnosis ($p=0.037$), tumor size ($p=0.028$), presence of metastases ($p=0.019$) and high-risk lesions ($p=0.036$). Survival at 1, 3 and 5 years was 87%, 71% and 61%, respectively. One year's mortality was significantly associated with tumor size ($p=0.021$), stage IV at diagnosis ($p=0.003$), non-complete resection ($p=0.002$) and palliation with imatinib ($p=0.035$). Similar associations were observed at the 3 and 5 years.
**Conclusion:** In the imatinib era there is an increased long-term survival in comparison with previous epidemiological data, and reduced recurrence rates. In more advanced cases survival remains limited in the short term.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1030 FEASIBILITY OF PRECUT COAGULATION WITH AN ENDO-KNIFE ALONE ON GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: A CASE-CONTROL STUDY


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**Introduction:** Intraoperative bleeding is a serious problem during gastric endoscopic submucosal dissection. The presence of a clear view, without bleeding, during the procedure helps the surgeon monitor the progress, and prevents injuries ulcer base or perforation by over-coagulation. Precut coagulation (PCC) with hemostatic forceps is reported to be effective to reduce intraoperative bleeding. Otherwise, this method involving the frequent replacement of devices, the use of PCC with knife alone would ensure a smoother procedure.
**Aims & Methods:** We aimed to assess the effectiveness of PCC with endo-knife alone at a super-low output setting. In this case-control study, we compared the hemostasis condition during ESD in 40 pairs of consecutive superficial gastric lesions that were treated via PCC with Hemostatic forceps (Control group) or the Flush knife BT at a super-low output setting (Knife group). The primary outcome was the frequency of major bleeding. The secondary outcomes included procedure time, en bloc resection rate, and adverse event rate.
**Results:** The average frequency of major bleeding was no significant difference between Group C and Group F ($1.30 \pm 1.30$ vs. $1.60 \pm 1.34$, $p=0.35$). The procedure time, the en bloc resection rate, and adverse event rates were similar in both groups. Lesions located at the upper-third of the stomach required the repeated hemostasis ($p=0.01$).
**Conclusion:** The use of PCC with the Flush knife BT alone, at a super-low output setting, prevented serious intraoperative bleeding in the same as using hemostatic forceps. Hence, this technique could ensure a smooth and safe procedure during gastric ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1031 SEROLOGIC SCREENING IN DIAGNOSTICS OF GASTRIC PRECANCEROUS CONDITIONS AND EARLY GASTRIC CANCER (EGC)


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**Introduction:** Multifocal atrophic gastritis (MAG) is considered to be precancerous conditions and associated with an increased risk for gastric cancer. To diagnose MAG and establish its extent, three methods can be used: endoscopy, histological assessment of biopsy specimens, and serology. Serum analysis of PG 1, G-17 and *H. pylori* antibodies (GastroPanel, Biohit), has been considered to be the promising tool for screening of precancerous conditions and early cancer of the stomach (1).
**Aims & Methods:** To assess the accuracy of non-invasive screening of atrophic gastritis (AG) and EGC with use of biomarkers compared to endoscopy and histology. We saved up 7 years' experience of investigation of patients with gastric dyspepsia, serum samples were obtained from 635 dyspeptic patients followed by high-resolution chromoendoscopy with biopsy sampling from antrum and corpus. The specimens of serum were investigated for IgG *H. pylori*, G-17 and PG I using the GastroPanel. The statistical analysis is made by MedCalc V9. After histology examination all patients were selected into 3 groups: AG ($n=252$), non-atrophic gastritis (NAG) ($n=352$) and EGC ($n=31$). Patients with AG were divided into antrum AG (AAG), $n=202$, and MAG, $n=50$.
**Results:** The dispersion analysis revealed that the PG 1 in patients with EGC ($45.02 \pm 8.23$) was lower than in the groups of patients with NAG ($114.02 \pm 8.0$) and AG ($82.70 \pm 6.60$), $p < 0.05$, in cases with AAG ($97.95 \pm 7.39$) it was higher than in the MAG group ($46.23 \pm 7.05$), $p < 0.05$. G-17 level in patients with EGC ($21.07 \pm 3.06$) was higher than in the groups of patients with NAG ($12.67 \pm 2.04$) and AG ($9.14 \pm 1.66$), $p < 0.05$. In patients with AAG the G-17 level - $7.74 \pm 1.65$ and in the MAG - $19.95 \pm 4.70$ respectively, $p=0.005$. There are no differences between biomarkers levels in patients with MAG and EGC. Distinctions the biomarkers at patients depending on process localization (body, antrum) and type a gastric cancer (intestinal, diffusion) it wasn't received. MAG was diagnosed in all patients with EGC, that's why the assessment of diagnostic accuracy of serological method was performed in this group. ROC-analysis determined that G-17 as well as PG 1 authentically diagnose MAG: G-17 AUC = 0.737, SE = 0.0862, 95%CI 0.590–0.805, PG 1 AUC = 0.779, SE = 0.0646, 95%CI 0.647- 0.850.

**TABLE 1:** Criterion values and coordinates of the ROC curve (MAG)

| Criterion | Sensitivity | 95% CI | Specificity | 95% CI |
|---|---|---|---|---|
| G-17 > 9.3 | 70.29 | 36.2–87.1 | 74.55 | 59.3–84.1 |
| PG 1 ≤ 64 | 80.57 | 50.6–95.1 | 62.78 | 47.9–74.1 |

**Conclusion:** Level of PG 1 ≤ 64 and G-17 > 9.3 have been shown as accurate biomarkers for MAG associated with high risk for gastric cancer. GastroPanel is currently being used to enhance the yield of endoscopic screening programs designed to identify individuals with high cancer risk who are indicated to undergo endoscopic examination.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1032 ENDOSCOPIC RESECTION FOR DUODENAL SUBEPITHELIAL TUMORS: A SINGLE-CENTER EXPERIENCE

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**Introduction:** Subepithelial tumors (SETs) in the gastrointestinal tract are often incidentally found during endoscopic examinations. Although the utility and safety of endoscopic resection (ER) of SETS in the esophagus and stomach have been described, data about the ER of duodenal SETs remain scant. Therefore, we aimed to investigate the clinical outcomes associated with the ER of duodenal SETs, and to assess possible predictive factors for incomplete resection.
**Aims & Methods:** We conducted a retrospective observational study of 62 patients (64 lesions) that underwent ER of duodenal SETs between June 2005 and December 2015 at the Pusan National University Hospital. The therapeutic outcomes from endoscopic submucosal dissection (ESD) and procedure-related complications were analyzed.
**Results:** Endoscopic mucosal resection (EMR) was performed in 38 tumors, EMR with a ligation device (EMR-L) in 18, and endoscopic submucosal dissection (ESD) in 8. The overall en-bloc resection and complete ER rates were 96.9% (62/64) and 100% (64/64), respectively. The complete pathologic resection rate was 76.6% (49/64). Multivariate logistic regression analyses determined that the macroscopic type (Yamada type I or II; odds ratio [OR] 6.460, 95% confidence interval [CI] 1.569–37.458, P = 0.027) and the treatment method (ESD; OR 7.178, 95% CI 1.291–39.323, P = 0.024) were independently associated with incomplete pathologic resection. The procedure-related bleeding and perforation rates were 6.3% and 4.7%, respectively. No recurrences were observed in patients who had undergone complete ER at a median follow-up period of 20 months (range, 6–112 months).
**Conclusion:** In conclusion, ER is an effective, safe, and feasible treatment for duodenal SETs, especially when the SET is located in the deep mucosal layer and/or the submucosal layer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1033 QUALITY OF LIFE OUTCOMES AFTER ENDOSCOPIC AND SURGICAL TREATMENT OF EARLY GASTRIC CANCER: A PROSPECTIVE COHORT STUDY.

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**Introduction:** Literature on the comparison of quality of life (QOL) in patients who have undergone endoscopic resection (ER) and surgical treatment is limited. We evaluated changes in the QOL after treatment for early gastric cancer (EGC), and compared these changes by the treatment procedure (endoscopic resection [ER] vs. surgery).
**Aims & Methods:** We reviewed baseline characteristics and questionnaire results of patients who underwent ER or surgery for EGC that were prospectively collected by the Korean Gastric Cancer Cohort study. The validated Korean version of the European Organization for Research and Treatment of Cancer 30-item core QOL questionnaire and its gastric module were used. We compared the QOL outcomes at pretreatment, and 1 year and 2 years after ER and surgery.
**Results:** In this study, 2.283 patients were included; 542 and 1.741 patients underwent ER and gastrectomy, respectively. Patients in the ER group were more likely to report a better QOL, except for the global QOL, after treatment than those in the surgery group. All the symptom domains were better in the ER group in terms of the absolute score and symptomatic percentage. In the surgery group, role functioning, diarrhea, dysphagia, eating restriction, anxiety, and body image scores deteriorated at 1 year and recovered at 2 years, except diarrhea did not recover to the baseline level. In the ER group and the surgery group, a high proportion of patients generally suffered from anxiety throughout the follow-up period. In the surgery group, the percentage of symptoms such as diarrhea, dysphagia, eating restriction, body image, and pain (gastric module) increased at 1 year and decreased at 2 years postoperatively, but not to the baseline level. Although the global QOL significantly improved postoperatively, patients who underwent ER had slight improvement at 1 year but deterioration at 2 years.
**Conclusion:** ER for EGC results in a better QOL than surgery, specifically in terms of symptom-related QOL, not the global QOL. Therefore, physicians should not ignore the global QOL of patients with EGC after ER, even if the patients received noninvasive treatment and had fewer symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1034 CLINICAL USEFULNESS OF MAGNIFYING ENDOSCOPY FOR NON-AMPULLARY DUODENAL TUMORS

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**Introduction:** A recent increase of the number of case reports on primary non-ampullary duodenal tumor has coincided with advances in the field of endoscopic examination. However, there have been few reports about magnifying endoscopic findings for these tumors.
**Aims & Methods:** The aim of this study was to investigate the clinical usefulness of magnifying endoscopy using narrow-band imaging (ME-NBI) and crystal violet (pit pattern) for non-ampullary duodenal tumors. We enrolled consecutive 103 patients with 103 primary non-ampullary duodenal tumors which were observed by ME-NBI and pit pattern before endoscopic resection at Hiroshima University Hospital until December 2014. Images of ME-NBI were

classified into 2 grades (Type B or Type C) according to the Hiroshima classification (Gastrointest Endosc 2009), and images of pit pattern were classified into 2 grades (regular or irregular). We retrospectively analyzed the clinicopathological features and endoscopic findings of ME-NBI and pit pattern between 2 histological grades according to the Vienna classification (Category 3; 73 tumors, Category 4; 30 tumors).
**Results:** The tumor size with Category 4 was significantly larger than that with Category 3 (Category 3; 10.0 mm vs. Category 4; 13.0 mm). There were no significant differences in location (incidence of second portion, Category 3; 73% vs. Category 4; 80%), and macroscopic type (incidence of depressed type, Category 3; 16% vs. Category 4; 26%) between 2 histological grade. In ME-NBI, Type C tumors with Category 4 (83%, 25/30) had significantly higher frequency than Type B tumors with Category 4 (17%, 5/30). In pit pattern, irregular tumors with Category 4 (77%, 23/30) had significantly higher frequency than regular tumors with Category 4 (23%, 7/30). The accuracy of Type C with ME-NBI for Category 4 was 87% (90/103), the sensitivity was 83% (25/30), the specificity was 89% (65/73), the positive predictive value (PPV) was 76% (25/33), and the negative predictive value (NPV) was 93% (65/70), respectively. The accuracy of irregular pit pattern for Category 4 was 84% (87/103), the sensitivity was 77% (23/30), the specificity was 88% (64/73), the PPV was 72% (23/32), and the NPV was 90% (64/71), respectively. There were no significant differences between ME-NBI and pit pattern for diagnosing histological grade. The accuracy, sensitivity, and specificity of Type C for Category 4 were 89% (75/84), 82% (18/22) and 92% (57/62) in flat elevated/protruded type, and 79% (15/19), 88% (7/8) and 73% (8/11) in depressed type, respectively. On the other hand, the accuracy, sensitivity, and specificity of irregular pit pattern for Category 4 were 87% (53/84), 82% (18/22) and 89% (55/62) in flat elevated/protruded type, and 74% (14/19), 63% (5/8) and 82% (9/11) in depressed type. There was no significant difference for diagnosing histological grade between ME-NBI and pit pattern, regardless of macroscopic type.
**Conclusion:** Our study showed that ME-NBI and pit pattern had the equivalent diagnostic ability for diagnosing histological grade of non-ampullary duodenal tumors. ME-NBI may be more useful because of its simple procedure without time consuming.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1035 LONG NONCODING RNA MALAT1 PROMOTES AGGRESSIVE GASTRIC CANCER THROUGH MMP1 OVER-EXPRESSION AND TRANSCRIPTIONALLY ACTIVATED BY C-JUN

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**Introduction:** Recently long non-coding RNAs (lncRNA) have emerged as new gene regulators and prognostic markers in several cancers including gastric cancer (GC), however, the detailed mechanisms remain largely unknown. In this study, we investigated the contributions of the lncRNA MALAT1, a highly conserved long noncoding RNA, in GC progression and its role in posttranscriptional regulation.
**Aims & Methods:** We analyzed MALAT1 expression levels by real-time reverse transcription PCR in 100 gastric tissues (50 GC tissues and 50 adjacent normal mucosa), and in four GC cell lines compared with epithelial cells. Transient RNAi-mediated knockdown and pcDNA-mediated overexpression of MALAT1 was performed. Stable shRNA-mediated knockdown and lentiviral-mediated overexpression of MALAT1 was to study the role of MALAT1 on in vivo tumorigenicity and metastatic burden in the context of xenograft assays. Proteomic profiling was performed to decipher differential protein expression in cells with different MALAT1 expression levels. One of the differentially regulated proteins, MMP1 was subsequently validated and its function evaluated through xenograft assays.
**Results:** We found that MALAT1 expression was higher in human GC tissues where it was associated with reduced patients' survival. MALAT1 silencing decreased GC cell proliferation and invasion and increased apoptosis. Mechanistic investigations showed that MALAT1 was transcriptionally activated by c-Jun and that it interacted with MMP1. MMP1 and MALAT1 had a positive relationship, both at expression level and in function. Direct interaction between the two was confirmed through RNA immunoprecipitation coupled with quantitative real time PCR. MMP1 was confirmed to be promoter of GC pathogenesis and as functionally similar to MALAT1 lncRNA.
**Conclusion:** MALAT1 expression may serve as a potentially important disease biomarker for the identification of highrisk GC patients. Moreover, our findings provide mechanistic evidence for MALAT1 over-expression and the ensuing malignant phenotype in both cultured and xenografts GC cells.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1036 ELEVATED PRC1 IN GASTRIC CARCINOMA EXERTS ONCOGENIC FUNCTION AND IS TARGETED BY PIPERLONGUMINE IN A P53-DEPENDENT MANNER

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**Introduction:** Gastric cancer is one of the most common malignancies worldwide and the second most frequent cause of cancer-related death in China. Protein regulator of cytokinesis 1 (PRC1) is involved in cytokinesis and plays key roles in microtubule organisation in eukaryotes.
**Aims & Methods:** This study was aimed to analyze the expression and to investigate the functional role of PRC1 in gastric tumorigenesis. The expression of PRC1 was evaluated by qRT-PCR, Western blot and immunohistochemistry. The biological function of PRC1 was determined by CCK-8 proliferation assays, monolayer colony formation, xenografted nude mice and cell invasion assays by shRNA-mediated knockdown in AGS and HGC27 cells. The regulation of PRC1 expression by piperlongumine was also investigated.
**Results:** PRC1 was up-regulated in primary gastric cancers. Overexpression of PRC1 in gastric cancers was associated with poor disease specific survival and overall survival. PRC1 knockdown in AGS and HGC27 cell lines suppressed proliferation, reduced monolayer colony formation, inhibited cell invasion and migration ability, and induced cell cycle arrest and apoptosis. PRC1 depletion selectively postponed cytokinesis in AGS cells instead of in HGC27 cells possibly due to the induction of GADD45a in AGS cells. Inhibition of PRC1 also suppressed tumor growth in vivo. We finally demonstrated that piperlongumine targets PRC1 via a p53-dependent manner in gastric cancers, thus suggesting that PRC1 is a novel downstream target of piperlongumine in gastric cancer.
**Conclusion:** Our findings supported the oncogenic role of PRC1 in gastric carcinogenesis. PRC1 might serve as a prognostic biomarker and potential therapeutic target for gastric cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1037 HOW DO INTRENATIONAL GASTRIC CANCER PREVENTION GUIDELINES REFLECT TO CLINICAL PRACTICE GLOBALLY?

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**Introduction:** Various clinical guidelines**,** including Kyoto global consensus are recommending particular steps, including 'search-and-treat' strategy for *H. pylori* to prevent gastric cancer, however little of this has been implemented to clinical practice.
**Aims & Methods:** The aim of the study was to identify how much of these recommendations have penetrated to practice. A web-based questionnaire was develop and distributed globally via number of international organizations and national professional societies. Questionnaire was available online for 5 months (October 2015 - February 2016) in three languages - English, Russian and German.
**Results:** Altogether 886 responses from 75 countries were received; of the responders 570 (64%) were men; mean age 47 years. There were 606 gastroenterologists and 65 epidemiologists among the responders. The majority were involved in cancer screening (66%), performing endoscopies (67%), and prescribing *H. pylori* eradication therapies (83%). Altogether 79.8% of the responders disagreed that the burden of gastric cancer is a disappearing problem and is not requiring any active intervention. 'Search-and-treat' strategy in the responder's country was considered appropriate by 44.4%, inappropriate – by 24.3%, but 31.3% of the responders were unsure. No difference between gastroenterologists (46.9% positive responses) and epidemiologists (45.5%) was revealed ($p = 0.84$). Population-based screening for gastric cancer was considered appropriate in the respective home-country by 62.2%, in other areas, but not the home-country – by 27.6%, but inappropriate – by 10.2% of the responders. Pepsinogen detection was considered an appropriate screening strategy by 26.1% of the responders, inappropriate – by 50.3%, but the remaining 23.6% considered it useful only in particular settings. No differences were observed in the responses of gastroenterologists and epidemiologists. When asked about volatile marker testing in exhaled air, only 23.4% considered that this approach is readily applicable for gastric cancer screening purpose; the major reason for this response was insufficient evidence (53.3%). The attitude towards *H. pylori* vaccination was as follows: 4.6% of the responders were eager to start vaccination immediately, 55.9% were supporting vaccination, but considered that more data is required; 12.0% were negative, but 27.6% did not have the opinion.
**Conclusion:** In general, the attitude of the specialists corresponds well to the guidelines, yet not always to the clinical practice, in particular in the case of 'search-and-treat' strategy. No substantial differences in the attitude were revealed between gastroenterologists and epidemiologists. Funding. The research was conducted within the HORIZON 2020 project SNIFFPHONE and was supported from the Project No.4 of National Health Program in Latvia BIOMEDICINE 2014–2017.
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## P1038 POTENTIALLY FUNCTIONAL POLYMORPHISMS IN METHIONYL-TRNA SYNTHETASE RELATED GENE ARE ASSOCIATED WITH GASTRIC CANCER IN A CHINESE POPULATION

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**Introduction:** Methionyl-tRNA synthetase (MARS) are responsible for cellular protein synthesis and cell viability in various process of tumorigenesis. We hypothesized that genetic variants in MARS might play an important role in the development of gastric cancer.
**Aims & Methods:** A case-control study was conducted including 2211 gastric cancer cases and 2266 cancer-free controls to evaluate the associations of 13 potentially functional polymorphisms in MARS with gastric cancer risk.
**Results:** We found significant associations with the risk of gastric cancer for rs511752 [odds ratio (OR) 0.85, 95% confidence interval (CI): 0.76–0.96, P = 6.21E-03]; rs542278 (OR = 0.84, 95% CI: 0.75–0.95, P = 6.80E-03) and rs508904 (OR = 0.88, 95% CI: 0.78–0.99, P = 3.15E-02). We further observed significant multiplicative interactions between rs511752 and drinking (P = 0.041). Combined analysis of these three SNPs showed a significant allele-dosage association between the number of risk alleles and gastric cancer risk (P for trend = 1.91E-4). Compared with individuals with "0–2" risk alleles, those carrying"3," "4," or "5 or more" risk alleles had a 1.32, 1.48, or 1.60 folds risk of gastric cancer, respectively.
**Conclusion:** These findings indicate that genetic variants in MARS might modify the individual susceptibility to gastric cancer in Chinese population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1039 LNCRNA HOTAIR ACTS AS A COMPETING ENDOGENOUS RNA TO PROMOTE CISPLATIN RESISTANCE IN GASTRIC CANCER VIA MIR-126/PI3K/ AKT/ MRP1 PATHWAY

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**Introduction:** Long non-coding RNAs (lncRNAs) have been reported to be involved in many cancer pathological conditions, including cisplatin resistance. However, the function of lncRNA-HOTAIR in cisplatin resistance for gastric cancer (GC) remain elusive. The aim of the study is to identify a novel mechanism that HOTAIR regulates the sensitivity of GC cells to cisplatin.
**Aims & Methods:** HOTAIR expression in GC cells and tissues was quantified by quantitative reverse transcription-PCR (qRT-PCR). The GC cell lines were transfected with pc-HOTAIR, si-HOTAIR, or their respective controls and we investigated the formation of cisplatin resistant phenotype of GC cells and possible molecular mechanisms.
**Results:** We found that HOTAIR was significantly up-regulated in cisplatin resistant GC cells and GC tissues compared with parental GC cells and non-cancerous gastric tissues. Besides, overexpression of HOTAIR could enhance proliferation, decrease apoptosis, and promote G1/S transition in GC cells. Furthermore, HOTAIR was found to directly bind to miR-126, promote miR-126 targets VEGFA and PIK3R2, then activate PI3K/AKT/MRP1expression.
**Conclusion:** Our findings revealed that HOTAIR can act as a competitive endogenous RNA to promote cisplatin resistance in GC and it will be a valuable predictor for treatment and target for reversal of cisplatin resistance in human GC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1040 NUCLEAR EXPRESSION OF MASPIN CORRELATES WITH POOR PROGNOSIS IN PATIENTS WITH GASTRIC CANCER AND IS AS A POSSIBLE INDUCTOR OF EPITHELIAL MESENCHYMAL TRANSITION

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**Introduction:** Maspin (mammary serine protease inhibitor) is a member of the serine protease inhibitor family that was previously proved by our team to exert p53-mediated pro-proliferation or tumor suppressor roles in several epithelial tumors such as colorectal, gastric carcinomas, or Merkel cell carcinoma. Its role is exerted based on the subcellular location in the cancer cells but the exact pathomechanism is unknown.
**Aims & Methods:** The aim of this study was to explore the possible role of maspin in epithelial mesenchymal transition (EMT), based on its expression in the tumor core and tumor front. Methods: We performed a retrospective analysis of 333 consecutive cases diagnosed between 2003–2012 in three departments of Pathology from Romania, Hungary, and Poland. The grade of tumor cells discohesivity was counted based on the number of tumour cells clusters in the invasion front, similar to the budding quantification in the colorectal cancer. The immunohistochemical (IHC) stains were done with Maspin and the following EMT-related antibodies: E-cadherin, N-cadherin, $\beta$-catenin, SLUG, and the stem cells marker CD44. The IHC quantification was performed in the tumor core and the invasion front.
**Results:** In the tumor core, Maspin was negative in 24.92% (n = 83) of the cases and presented nuclear only expression in 15.31% (n = 51) of the cases. The other cases revealed cytoplasm only positivity (26.13%) or mixed cytoplasm and nuclear Maspin expression (33.64%), independently by the pT stage. The Kaplan-Meier survival analysis showed that nuclear only expression of maspin and lymph node metastases were independent indicators of poor prognosis and low survival in patients with gastric cancer. Nuclear only expression in the tumor core and tumor front were correlated with presence of lymph node metastases ($p < 0.0001$), high grade of discohesivity in the invasion front ($p = 0.01$), E-cadherin loss in the invasion front ($p = 0.001$), nuclear expression of $\beta$-catenin in both core ($p = 0.002$) and front ($p = 0.02$), and CD44 positivity in more than 50% of the tumor cells ($p = 0.003$). SLUG expression was seen in 306 out of the 333 cases (91.89%) and N-cadherin in 67 of the cases (20.12%) without correlation with the other examined markers.
**Conclusion:** This is the first report revealing a possible role of nuclear maspin in EMT of gastric cancer cells. It can explain the negative prognostic role of nuclear maspin in these carcinomas and might serve as a predictive marker for EMT inhibition.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1041 POPDC1/BVES AND POPDC3 ARE DOWNREGULATED IN GASTRIC INTESTINAL METAPLASIA

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**Introduction:** The Popeye domain containing (POPDC) gene family comprises three highly conserved, developmentally-regulated transmembrane proteins, POPDC1–3 (1). POPDC1/BVES (also called blood vessel epicardial substance) and POPDC3, encode proteins that regulate cell-cell adhesion and cell migration during epithelial-mesenchymal transition. POPDC1/BVES and POPDC3 were recently found to be downregulated in gastric carcinoma in humans and have been linked to the mechanism of gastric tumorogenesis (2).

**Aims & Methods:** Aims: In this work, we examined the possibility that POPDC1/BVES and POPDC3 may serve as predictive markers for gastric tumorogenesis and analyzed the expression levels of these genes in intestinal metaplasia, a premalignant stage of gastric carcinoma. Methods: mRNA was isolated from formalin fixed paraffin embedded endoscopic gastric biopsies of 16 normal, 24 intestinal metaplasia, and 8 carcinoma patients. Only *Helicobacter pylori* negative biopsies from the gastric antrum were included in the study. The expression levels of POPDC1/BVES, POPDC3 as well as CDX2 (a biomarker for gastric premalignancy) were assessed by quantitative RT-PCR using RPLP0 as the normalizing mRNA. The biopsies were also stained for POPDC1/BVES.

**Results:** Compared to normal biopsies, we found a statistically significant reduction in the expression levels of POPDC1/BVES and POPDC3 in intestinal metaplasia as well as in the carcinoma biopsies. The expression levels of CDX2 were elevated in both, the intestinal metaplasia and the carcinoma biopsies. Correlation analysis indicated a high correlation between POPDC1/BVES and POPDC3 transcript levels whereas a negative correlation was found between the levels of POPDC1/BVES and CDX2 mRNA transcripts. Preliminary evaluation of POPDC1/BVES immunostaining suggested lower incidence of POPDC1/BVES labeling in the luminal surface of gastric glands of intestinal metaplasia, compared with normal tissues.

**Conclusion:** This is the first demonstration that POPDC1/BVES and POPDC3 are downregulated in intestinal metaplasia suggesting them as potential players in and biomarkers for gastric tumorogenesis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1042 TARGETING ALDEHYDE DEHYDROGENASE 2 FOR PREVENTION OF GASTRIC CANCER IN ESTABLISHED RISK GROUP

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**Introduction:** Acetaldehyde is a key cause of alcohol hangover symptoms and a well known Group 1 carcinogen to humans (WHO). It is metabolized by Aldehyde dehydrogenase (ALDH2), which is genetically deficient in 30–50% of Eastern Asians. Local acetaldehyde exposure to gastric mucosa is a key event in the pathogenesis of gastric cancer. It is closely associated with major risk factors, including alcohol drinking, ALDH2 deficiency, achlorhydria, *H. pylori* infection, and tobacco smoking. Recently, a variety of anti-hangover products are commercially available, however, almost none of them has been proven to show enhanced metabolizing capacity of ALDH 2 in a live subject.

**Aims & Methods:** We aimed to test a specific anti-hangover product of interest. The enzyme activities of the anti-hangover substance were examined by in-vitro & in-vivo experiments to measure the amount of NADH formation which is generated through catalytic conversion of alcohol and acetaldehyde, by using a spectrophotometer at 340 nm. Powder sample of a commercial anti-hangover product (South Korea) was used as the experimental substance. In-vivo examination tested the ethanol and acetaldehyde concentration in blood of rats with oral infusion of experimental substance before or after ethanol intake. In first test, twenty four SD male rats were randomly assigned into one of four groups: group1 received only saline, group2 was subjected to ethanol only, group 3 received ethanol with substance (73 mg/kg), and group 4 ethanol with substance (220 mg/kg). Oral dosing of 50% ethanol (3 g/kg body weight) was given 30 minutes after substance gavages, followed by time-dependent collection of rat's blood when zero, 1, 3, 5, and 8 hours after dosing of ethanol. In second test, similar examination was repeated with two groups including ethanol only ($n = 6$) and ethanol with substance (220 mg/kg) ($n = 6$). The differentiator of second in-vivo test was that experimental substance be given 1 hr after ethanol gavage, approximately near maximum level of blood acetaldehyde.

**Results:** In vitro measurements of the activities of alcohol dehydrogenase & aldehyde dehydrogenase within the anti-hangover substance were 1.84 unit/g and 0.28 unit/g, respectively. The enzyme activities in rats' blood under the substance that was given 30 minutes before ethanol intake are as follows: after 1 hour of ingestion of ethanol, the concentration of ethanol in blood showed maximum values for all testing group, but decreases by 15.5% ($p < 0.246$) and 28.3% ($p < 0.011$) were observed for testing groups of dosing substance 73 and 220 mg/kg, respectively. In the case of a group with dosing 220 mg/kg, meaningful decrease in the concentration of ethanol through all measurement times was observed compared to a group of ingestion of ethanol only. With acetaldehyde level in blood, the maximum values for all testing groups were measured 1 hr after ethanol ingestion, demonstrating no significant differences among testing groups. However, the concentration of acetaldehyde in blood for ethanol only group started to decease after 3 hours, in contrast, those of groups with anti-hangover substance have shown concentration-dependent reduction after one hour. As for a group of dosing substance 220 mg/kg, meaningful level of decreases were observed after 3 hours ($p < 0.01$) and 5 hours ($p < 0.05$). Finally, the cases with oral intake of substance 220 mg/kg after 1 hr of ethanol intake have shown more significant and obvious decreases in blood acetaldehyde concentration through the period of all measurement times.

**Conclusion:** Oral intake of anti-hangover substance has significantly enhanced alcohol or acetaldehyde-metabolizing capacity in rat model, potentially suggesting increased ALDH 2 capacity within circulation. Using this substance, further animal researches on prevention of gastric cancer are recommended to conduct.

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All other authors have declared no conflicts of interest.

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## P1043 CORRELATIONS AMONG PH OF GASTRIC JUICE, ATROPHIC GASTRITIS, INTESTINAL METAPLASIA AND H. PYLORI INFECTION

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**Introduction:** Gastric mucosa undergoes a series of changes including of chronic gastritis, atrophic gastritis, intestinal metaplasia and dysplasia, before progressing into gastric cancer, in which process *H. pylori* infection plays a major role. As pH measurement of gastric juice is very difficult, there is rare report regarding the relationship between this process and acid secretion.

**Aims & Methods:** The aim of this study is to evaluate the correlations among pH of gastric juice, atrophic gastritis, intestinal metaplasia, pepsinogen I/II ratio, *H. pylori* infection and clinical diagnosis. From October 2005 to March 2013, a total of 46 subjects were enrolled. Gastric biopsies and stomach juices were collected from subjects who underwent standard endoscopy at Seoul National University Bundang Hospital. Histological atrophic gastritis (AG) and intestinal metaplasia (IM) were assessed by updated Sydney system in the body and antrum, respectively. *H. pylori* infection was determined by any one of modified Giemsa stain, CLOtest and culture. We categorized gastric juice pH as $pH < 3$ ($n = 28$) and $pH \geq 3$ ($n = 18$) because the subject number was small. Pepsinogen test was performed by determined using a latex agglutination method (HBi Corp, Seoul, Korea).

**Results:** *H. pylori* infection state was found significantly lower in the $pH < 3$ group (21.4%) than that of $pH \geq 3$ group (Table). However, the clinical diagnosis was not different in the two gastric pH groups. The subjects with $pH \geq 3$ in gastric juice showed AG in the body more frequently than $pH < 3$ group ($p = 0.047$) (Table). However, this difference was not found in case of antral AG. Similarly, subjects with $pH \geq 3$ in gastric juice showed IM in the body more frequently than $pH < 3$ group ($p = 0.051$). However, this difference was not found in case of antral IM. Pepsinogen I/II ratio did not show any correlation with pH of gastric juice.

**Table:** Characteristics of 46 subjects

| Variables | pH < 3 (n = 28) | pH ≥ 3 (n = 18) | p-value |
|---|---|---|---|
| pH (mean ± SD) | 1.79 ± 0.45 | 5.46 ± 1.58 | |
| M/F, n (%) | 19/9 (67.9/32.1) | 15/3 (83.3/16.7) | 0.243 |
| Age (mean ± SD), years | 58.5 ± 13.7 | 56.0 ± 11.1 | 0.522 |
| *H. pylori* infection state | 6 (21.4%) | 11 (61.1%) | **0.007** |
| Clinical diagnosis | | | 0.332 |
| Control, DU, BGU | 10 (35.7) | 4 (22.2) | |
| Gastric dysplasia/cancer | 18 (64.3) | 14 (77.8) | |
| Atrophic gastritis | | | |
| Antrum | n = 20* | n = 14 | 0.738 |
| Present, n (%) | 10 (50) | 8 (57.1) | |
| Body | n = 19 | n = 17 | **0.047** |
| Present, n (%) | 4 (21.1) | 9 (52.9) | |
| Intestinal metaplasia | n = 28 | n = 18 | |
| Antrum | | | 0.318 |
| None or mild, n (%) | 21 (75) | 11 (61.1) | |
| Moderate or severe, n (%) | 7 (25) | 7 (38.9) | |
| Body | | | **0.051** |
| None or mild, n (%) | 23 (82.1) | 10 (55.6) | |
| Moderate or severe, n (%) | 5 (17.9) | 8 (44.4) | |
| Pepsinogen I/ II ratio | n = 22 | n = 15 | 0.464 |
| (mean ± SD) | 3.87 ± 1.35 | 3.05 ± 1.94 | |

DU: duodenal ulcer; BGU: benign gastric ulcer *Remaining 8 subjects showed inapplicable finding for histological atrophic gastritis.

**Conclusion:** *H. pylori* infection affected gastric juice pH, which showed good relationship with AG and IM in the body. These results suggest of close relationship of *H. pylori* infection on the acid secretion by way of AG and IM in the body.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1044 POTENTIAL ROLE OF MICRORNA-126 IN THE DIAGNOSIS OF CANCERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** Cancer has become a major public concern all over the world and early diagnosis of cancer is of great benefit for treatment and prognosis. Several studies have investigated the association between abnormal circulating microRNA-126 (miR-126) expression and the risk of various cancers, but the results are inconsistent. Therefore, this meta-analysis was carried out to assess the potential diagnostic value of miR-126 for cancer.
**Aims & Methods:** Relevant studies were searched from PubMed, Embase, and Web of Science and we calculated the pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and area under the summary receiver operator characteristic curve (AUC) to assess the diagnostic value of miR-126 for cancer detection.
**Results:** A total of 745 cancer patients and 749 controls from 11 studies of 7 papers were contained in this meta-analysis. The summary estimates revealed that the pooled sensitivity was 68% (95% confidence interval (CI): 60%-75%), the specificity was 76% (95% CI: 65%-85%), the PLR was 2.87 (95% CI: 1.96–4.21), the NLR was 0.42 (95% CI: 0.35–0.52), the DOR was 7 (95% CI: 4–11), and the AUC was 0.77 (95%CI: 0.73–0.80). Moreover, the sample type, cancer type, sample size, and quality score might be sources of heterogeneity.
**Conclusion:** Results from this systematic review and meta-analysis suggested that miR-126 had great potential to be a noninvasive biomarker in the diagnosis of cancer. However, more well-designed studies with larger sample size on the diagnostic value of miR-126 for cancer are needed in the future.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1045 POLYPOID LESIONS OF NON-TYPICAL VARICEAL MORPHOLOGY SEEN IN UPPER GI ENDOSCOPY, IN PATIENTS WITH PORTAL HYPERTENSION. OUTCOMES OF INVESTIGATION WITH ENDOSCOPIC ULTRASOUND

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**Introduction:** Gastroduodenal polypoid lesions are frequently seen in upper GI endoscopy in patients with portal hypertension (PH). Although in certain cases the appearance is typical of ectopic varices, in other cases the true nature of the visualized lesion remains uncertain. The optimal strategy to clarify diagnosis is not clearly defined.
**Aims & Methods:** The aim of this study was to investigate such lesions routinely with endoscopic ultrasound (EUS) and report the outcome of EUS assessment. All patients with PH referred for EUS due to uncertain polypoid lesions seen in upper GI endoscopy, between June 2008 and November 2015, were included. The degree of confidence regarding their true nature varied. Data on aetiology of PH, severity of cirrhosis (if present), demographic characteristics, lesion location, presence of other signs of PH, endoscopic impression and outcome of investigation with EUS and pathology (if appropriate/available) were retrospectively collected after reviewing the EUS reports and hospital electronic database. Final diagnosis was categorized in 3 main groups: 1. Varices, 2. Polyp with underlying vessel/varix and 3. Non-vascular lesions. Patients with known or confidently diagnosed varices at index endoscopy that were referred only to further assess the extent of portal hypertension or facilitate intervention for variceal obliteration were excluded.
**Results:** A total of 36 patients (26 male) were included. PH aetiology was alcoholic liver disease (ALD) or non-alcoholic fatty liver disease (NAFLD) in the majority of patients (83.3%). Most lesions were seen in distal stomach and duodenum (69.4%), while in almost all patients (94.4%) there were other findings of PH. Varices were found in 27.8% of patients, while an equal number were found to have polyps with underlying vessels. Comparing the presumed diagnosis at index endoscopy with the final EUS assisted diagnosis, revealed a poor ability to predict the actual nature of the lesion, since only 42.1% of lesions considered to be polypoid/neoplastic were found to be non-vascular under EUS and 50% of those considered to be submucosal lesions where confirmed as varices.
**Conclusion:** 1.The endoscopist should have a high index of suspicion regarding varices when performing endoscopy in patients with PH. 2. Obtaining biopsies in cases where the true nature of lesions is uncertain should be avoided, as in such cases it is impossible even for experienced endoscopists to accurately categorize them thus significantly increasing the risk of bleeding from varices.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1046 HEREDITARY HEMORRAGIC TELANGIECTASIA: CHARACTERIZATION OF A LARGE COHORT OF PATIENTS WITH DIGESTIVE MANIFESTATIONS

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**Introduction:** Hereditary haemorrhagic telangiectasia (HHT) is a rare autosomal dominant disease affecting 1 in 5000 habitants. It's characterized by the appearance of arteriovenous malformations (AVMs) at micro and macrovascular level, throughout the gastrointestinal (GI) tract, liver, lung and brain. As a result, in the setting of GI bleeding or liver function abnormalities these patients are often evaluated in our clinical practice.
**Aims & Methods:** We aimed at characterizing the phenotypic patterns and disease severity of a cohort of patients admitted, during the past 15 years, to a gastroenterology department of a tertiary medical centre. Medical records were reviewed for demographic, biochemical, endoscopic, radiological and genetic analysis variables collection.
**Results:** Nineteen patients with HHT according to the curacao criteria were identified. Mean age: 61.2 ± 17 years, mostly male (M/F:12/7). No previous diagnosis was present in 26.3% (n = 5) of patients. The vast majority (84% n = 16) reported epistaxis and 52% (n = 10) had at least one previous episode of GI bleeding. Angiodysplasias were distributed through the GI tract: upper 56% (n = 9/16); mid portion 87.5% (n = 7/8); lower 33% (n = 5/15). Visceral AVMs location: hepatic 58% (n = 10/17); pulmonary 27.2% (n = 3/11) and cerebral 33% (n = 3/10). A relevant proportion of our patients had not been submitted to complete endoscopic (16%) and organ (hepatic: 10%, pulmonay: 42% and cerebral: 47%) investigation. Laboratory abnormalities were mostly biochemical cholestasis 36.8% (n = 7) without aminotransferase changes. Portal hypertension: oesophageal varices 31% (n = 5/16); thrombocytopenia 21% (n = 4/19); ascites 44% (n = 8/18). Other complications: thrombotic events 25% (n = 4/16); visceral/articular abscess 15.7% (n = 3/19); idiopathic thrombocytopenic purpura 5.2% (n = 1). Genetic analysis was only available for 2 patients. Overall mortality was 36.8% (n = 7/19) with 10% (n = 2) directly consequence of a HHT complication.
**Conclusion:** This cohort of HHT patients demonstrates a high phenotypic variability as well as a non-negligible disease associated mortality within the specific group of patients with GI manifestations of HHT. It also highlights that there is a need for a protocol based approach in the evaluation and clinical care of this complex set of patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1047 MECHANISM UNDERLYING STRESS-RELATED MUCOSAL DAMAGE: UPPER OPTICAL GASTROSCOPY

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**Introduction:** The association between stress and gastrointestinal (GI) diseases are well established. The pathogenesis has not been completely clarified, but strong evidence points to disorders of neural and endothelial regulation of the upper GI tract as the major cause.

**Aims & Methods:** The aim: To study the adrenergic and nitroergic mechanisms underlying stress-related mucosal damage (SRMD). The study was carried out on mongrel rats (n = 96) with experimental model of SRMD and patients with erosive gastritis (EG, n = 27) and ulcer bleeding (UB, n = 30). Gastric blood flow was measured using Laser Doppler flowmetry. Nitric oxide (NO) level in epithelium of stomach was analyzed by spectrophotometry.

**Results:** Chronic (4 months) social stress (overpopulation) was accompanied by superficial mucosal damage and primarily erosions in 83% of rats (61 of 73). Additional daily stress (2 hours immobilization) during 1 month in all rats (n = 61) with stress-related injury (SRJ) induced development of stress-related ulcer bleeding (SRUB). In first step of our work we studied role of adrenergic system in development of SRMD. Submucosal infusion of phenylephrine, tyramine, yohimbine caused the drop in gastric blood flow which was the same in healthy rats and rats with SRI and SRUB. Submucosal infusion of isoproterenol induced dilation of gastric vessels which was 2-fold higher in rats with SRI and 5-fold greater in rats with SRUB vs. healthy group. In clinical study we found that patients with EG showed vasoconstriction after submucosal adrenaline injection in stomach but patients with UB – vasodilation. It is known that one of mechanisms underlying adrenomadiated vasorelaxation is activation of NO production. In second step of our work we studied role of NO system in development of SRMD. In rats with SRI and rats with SRUB level of NO in epithelium of stomach was 2-fold and 5-fold higher vs. healthy rats. In clinical study using endoscopic biopsy we found that NO level in epithelium of stomach was higher 1.5-fold in patients with EG and 4-fold greater in patients with UB. Submucosal infusion of L-NAME (10 mg/kg) caused long-term suppression of acid secretion in rats with SRJ and SRUB. NO blockade by L-NAME (10 mg/kg, per os) during 1 month in rats with SRI (n = 23) was accompanied by decrease in number of rats with SRUB (9 of 23).

**Conclusion:** Development of SRMD is accompanied by increase in vasodilator effect of adrenergic influences on stomach and increase in NO production in gastric epithelium. Blockers of NO synthesis may be the novel acid-suppressive pharmacological agents. The research was supported by Grant of Russian Ministry of Science and Education 17.488.2014 K.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1048 SUPERIOR MESENTERIC ARTERY SYNDROME: A TRUE AND MISDIAGNOSED CLINICAL ENTITY

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**Introduction:** Superior Mesenteric Artery Syndrome (SMAS) is a rare cause of duodenal obstruction, resulting from the compression of the third duodenum between superior mesenteric artery and aorta. Still most clinicians are not aware of this disease and patients are often misdiagnosed. Clinical presentation consists of aspecific gastrointestinal symptoms. The diagnosis is mostly reached by a process of exclusion and the clinical suspect needs to be confirmed radiologically by barium swallow and CT/MR angiography.

**Aims & Methods:** We propose our experience in 39 patients with history of chronical gastrointestinal disorders, who underwent surgical correction for SMAS. Aim of the study was to analyze clinical presentation and diagnosis of SMAS and to assess surgical outcome. Between October 2008 and March 2016 we prospectively collected demographic and clinical data of consecutive SMAS patients. Symptoms were scored on a Likert scale using a detailed questionnaire about abdominal pain, bloating, regurgitation, nausea, and vomiting. The diagnosis was assessed through barium swallow, CT/MR-angiography, endoscopy. Diagnostic criteria at angiogram are: aorto-mesenteric angle $\leq 22^{\circ}$, distance $\leq 8$ mm. All patients underwent duodenojejunostomy, with or without a distal resection of the duodenum. At follow up, symptom score and quality of life were evaluated and a barium swallow was performed.

**Results:** Thirty-nine patients (11 M/28 F, mean age $38 \pm 14$ years) complained of a long clinical history (mean 91 months; range 12–138) of aspecific digestive symptoms. Mean BMI was $17.9 \pm 2.8$, weight loss $9 \pm 7$ kg. Eight patients (21%) had been previously studied for GERD elsewhere and fundoplication had been performed; in 8 patients (21%), one or more bouts of acute pancreatitis had occurred. Once SMAS was suspected clinically, upper gastrointestinal series and CT/MR angiography confirmed the diagnosis. Barium swallow showed a gastroduodenal dilation in 17 cases (44%) and a slow contrast progression in 13 (33%); mean aorto-mesenteric angle was $12 \pm 6^{\circ}$, distance was $6 \pm 2$ mm. All patients underwent laparotomic duodenojejunostomy; in 32 of them (82%), a distal duodenum resection was added. Ten patients (26%) also underwent a fundoplication for GERD. Mortality was nil, while in 6 patients (15%) a complication occurred: melena (2), acute pancreatitis (2), intestinal obstruction by abdominal adhesion (1) and hemoperitoneum (1). In all patients a water-soluble contrast swallow was performed on postoperative day 6, and since no anastomotic leak was recorded, realimentation was started on mean postoperative day 7; patients were discharged after $11 \pm 7$ days. Barium swallow at 2 months showed a delayed gastroduodenal emptying in 10 patients (26%), while a wide and pervious anastomosis was demonstrated in all series (100%). At a mean follow-up of $34 \pm 16$ months, symptom score significantly dropped ($p < 0.0001$) and an increase in BMI ($p < 0.0001$) was recorded [Table].

| | Before Surgery | After Surgery | P value |
|---|---|---|---|
| Symptom Score | $34 \pm 10$ | $15 \pm 13$ | $< 0.0001$ |
| BMI (kg/m$^2$) | $17.9 \pm 2.8$ | $19.4 \pm 3.1$ | $< 0.0001$ |
| Weight gain (kg) | $-9 \pm 7$ | $6 \pm 1$ | $< 0.0001$ |
| PPI therapy | 29/39 (74%) | 12/39 (31%) | 0.0002 |
| Prokinetic therapy | 24/39 (62%) | 10/39 (26%) | 0.02 |

**Conclusion:** We suggest to consider SMAS as a differential diagnosis in subjects with aspecific digestive symptoms, especially if a clinical history of acute pancreatitis or surgical treatment for GERD is recorded. In patients with chronical upper gastrointestinal symptoms and a radiological diagnosis of SMAS, surgical bypass improves symptoms and quality of life.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1049 SUPERIOR MESENTERIC ARTERY SYNDROME AND ACUTE PANCREATITIS

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**Introduction:** Superior mesenteric artery syndrome (SMAS) is a rare cause of chronic duodenal obstruction, due to the compression by superior mesenteric artery and aorta on the third duodenum. Recent studies report SMAS as a rare cause of recurrent acute pancreatitis.

**Aims & Methods:** Thirty-nine consecutive SMAS patients were addressed to our Department between October 2008 and March 2016; eight of them complained of a past clinical history of acute pancreatitis. Demographic and clinical data were prospectively collected; previous surgical and endoscopic procedures were also recorded. Symptoms of SMAS were scored on a Likert scale using a detailed questionnaire about abdominal pain, bloating, regurgitation, nausea, and vomiting. The diagnosis was assessed through barium swallow, CT/MR-angiography, endoscopy. Diagnostic criteria at angiogram are: aorto-mesenteric angle $\leq 22^{\circ}$, distance $\leq 8$ mm. All patients underwent duodenojejunostomy with a distal resection of the duodenum. At follow up, symptom score was collected, quality of life was evaluated and a barium swallow was performed. Moreover, BMI, weight gain, serum lipase and amylase activity were also collected and considered in determining outcome. The aim of our study was to investigate the occurrence of acute pancreatitis in a larger group of patients who were surgically treated for SMAS, and to assess medical history and final outcome.

**Results:** Eight patients (1 M/7 F, mean age $42 \pm 16$ years) complained of a long clinical history (mean 57 months; range 12–78) of aspecific digestive symptoms and acute pancreatitis, presenting with 1 or more episodes of abdominal pain, nausea, vomiting and serum amylase increase. In 5 of these patients a cholecystectomy had been previously performed elsewhere, while 2 had undergone more than one endoscopic retrograde cholangiopancreatography (ERCP) with biliary sphincterotomy. After these procedures, patients still complained of abdominal pain, bloating, nausea, vomiting, regurgitation, dyspepsia and weight loss (mean $10 \pm 5$ kg); mean symptom score was $36 \pm 9$, BMI $16.5 \pm 2.6$. Barium swallow showed a gastroduodenal dilation in 5 cases (63%) and a slow contrast progression in 4 (50%); at CT/MR-angiography, mean aorto-mesenteric angle was $10 \pm 7^{\circ}$, distance was $6 \pm 4$ mm. All patients underwent a duodenojejunostomy with distal duodenum resection. Postoperative mortality was nil, while 2 complications occurred: an acute pancreatitis, successfully treated conservatively; and a small-bowel obstruction caused by adhesion formation, that required adhesiolysis. In all patients a postoperative water-soluble contrast swallow was performed, and since no anastomotic leak was recorded, they started realimentation on mean postoperative day 10 and were discharged after $14 \pm 8$ days. Barium swallow at 2 months showed delayed gastroduodenal emptying in 2 patients (25%) and regular anastomosal transit in all series (100%). At a mean follow-up of $31 \pm 14$ months, symptom score dropped to $15 \pm 11$ ($p < 0.05$) and an increase in BMI $18.4 \pm 3.9$ was recorded. No recurrence of acute pancreatitis occurred and pancreatic enzyme activity was normal in all patients.

**Conclusion:** The association of SMAS and recurrent acute pancreatitis is a rare but possible and potentially life-threatening condition. We suggest to consider SMAS as a differential diagnosis in patients with recurrent acute pancreatitis of unknown origin and aspecific digestive symptoms. In these patients, endoscopic papillotomy (ERCP) should not be performed; surgical treatment is indicated to relieve symptoms and improve quality of life.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00

**H. PYLORI II – POSTER EXHIBITION**

### P1050 ASSOCIATION BETWEEN HELICOBACTER PYLORI INFECTION AND EOSINOPHILIC ESOPHAGITIS: RESULTS OF A MULTICENTER PROSPECTIVE EUROPEAN STUDY

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**Introduction:** An inverse association between *Helicobacter pylori* (*H. pylori*) infection and esophageal eosinophilia has been lately suggested. However, data are based on retrospective studies or small prospective studies, with histology or serology as diagnostic tests for *H. pylori* infection.

**Aims & Methods:** Aims: to evaluate the association between *H. pylori* infection and eosinophilic esophagitis (EoE), whether this association was different between responders and nonresponders to PPI therapy, besides elucidating the existence of potential confounding factors for this association. Methods: Prospective multicenter case-control study conducted in Spain and Italy. Controls: patients undergoing upper endoscopy due to esophageal symptoms, without eosinophils on esophageal biopsies. Patients: EoE defined according to available guidelines. All EoE patients underwent an 8-week high-dose PPI trial. Patients with clinic and histologic remission (< 15 eos/HPF) on PPIs were defined as PPI-responsive esophageal eosinophilia (PPI-REE). Atopic status was defined by the presence of any of these conditions: asthma, rhinoconjunctivitis, food allergy, oral allergy syndrome, atopic dermatitis, anaphylaxis, urticaria or angioedema. Positive *H. pylori* infection: urea breath test, rapid urease test or histology. In case of negative results with invasive tests, a confirmatory urea breath test was performed.

**Results:** A total of 243 individuals [75 controls, 168 EoE patients (42% responders to PPI therapy) ] have been included. Compared to controls, EoE patients showed a significantly lower rate of *H. pylori* infection (28% vs. 43%, $p = 0.01$). No differences in *H. pylori* status were observed between responders and nonresponders to PPI therapy (29% vs. 26%, $p = 0.58$). The presence of atopic status was significantly higher in patients vs. controls (72% vs. 34%, $p < 0.001$) and in EoE patients vs. PPI-REE patients (65% vs. 42%, p 0.009). When individuals were stratified according to their atopic status, the rate of *H. pylori* infection was significantly higher in overall non-atopic vs. atopic individuals (49% vs. 23%, $p < 0.001$), controls (54% vs. 23%, p 0.009) and patients (43% vs. 22%, $p = 0.01$). *H. pylori* infection was significantly less common in atopic vs. non-atopic PPI-REE patients (19% vs. 44%, p 0.024). However, this difference could not be confirmed in non-atopic vs. atopic EoE patients (24% vs. 37%, p 0.2), because of the small numbers of non-atopic EoE patients.

**Conclusion:** An inverse association between *H. pylori* infection and EoE was confirmed. *H. pylori* infection was significantly more common in non-atopic controls and patients. These data suggest that the former inverse association might be casual, whereas the gastric microorganism may actually protect against atopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1051 SURVEILLANCE OF HELICOBACTER PYLORI RESISTANCE TO ANTIBIOTICS IN FRANCE IN 2014

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**Introduction:** The outcome of *Helicobacter pylori* eradication therapies is very much dependent on the antimicrobial susceptibility of the strains. Given the difficulty of offering tailored treatments in some areas, it is important to have accurate knowledge of the prevalence of *H. pylori* resistance which is evolving over time.

**Aims & Methods:** Our aim was to perform a survey of antimicrobial resistance in France in 2014. Gastric biopsy specimens obtained from patients during upper digestive endoscopy were sent to a central laboratory for *H. pylori* culture and antimicrobial susceptibility testing. A real-time PCR detecting the bacterium and the mutations leading to clarithromycin resistance was also performed.

**Results:** Seventy-five gastroenterologists, distributed throughout the different regions of France, enrolled 984 patients. Among the 783 patients with no previous eradication treatment, 266 (33.9%) were *H. pylori* positive. The strains showed high resistance to clarithromycin (22.2%), moderate to levofloxacin (15.4%), high to metronidazole (45.9%), very low to amoxicillin and rifamycin (<1%), and nil to tetracycline. There were 187 patients who received a previous *H. pylori* treatment, of which 115 were *H. pylori* positive. Among the 81 who received other treatment than Pylera®-proton pump inhibitor (PPI), 79% were resistant to clarithromycin, 17.3% to levofloxacin and 72.8% to metronidazole. The corresponding figures for the 34 who received Pylera®-PPI were 61.7%, 11.8% and 91.2%, respectively. None of the patients having received Pylera®-PPI developed resistance to tetracycline. Real-time PCR detected all *H. pylori* patients for whom culture was positive and 30 others. The mutations found were essentially A2142/2143G (150) while there were six A2142C and two A2142T. A double population (mutants + wild type) was observed in 21 cases.

**Results:** Seventy five gastroenterologists, distributed in the different regions of France, enrolled 984 patients. Among the 783 patients who never had eradication treatment before, 266 (33.9%) were *H. pylori* positive. The strains showed high clarithromycin resistance (22.2%), moderate to levofloxacin (15.4%), high to metronidazole (45.9%), very low to amoxicillin and rifamycin (<1%), and nil to tetracycline. There were 187 patients who received a previous *H. pylori* treatment, of which 115 were *H. pylori* positive with very high resistance to clarithromycin (73.9%) and metronidazole (78.3%). None of the patients having received Pylera®-proton pump inhibitor developed resistance to tetracycline. Real-time PCR detected all *H. pylori* patients for whom culture was positive and 30 others. The mutations found were essentially A2142/2143G (151) while there were five A2142C and two A2142T. A double population (mutants + wild type) was observed in 21 cases.

**Conclusion:** This study shows that *H. pylori* resistance to clarithromycin is still increasing and already above the threshold indicating an abandon of its use. However, the progression is slower than in the previous decade probably because of a more prudent use of antibiotics including macrolides during these last years.

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L. Bénéjat: no conflict of interest
E. Sifré: no conflict of interest
E. Bessède: no conflict of interest
P. Lehours: no conflict of interest
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### P1052 A DRAMATIC RISE IN CLARITHROMYCIN RESISTANCE OF HELICOBACTER PYLORI STRAINS AMONG CHILDREN IN LITHUANIA.

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**Introduction:** Primary resistance rates of *Helicobacter pylori* (*H. pylori*) to clarithromycin in Northern and Eastern Europe historically have been low; however, monitoring of antibacterial resistance is crucial for maintenance of effective regional treatment strategies.

**Aims & Methods:** The study evaluated primary antibiotic resistance of *H. pylori* strains in adults and children in Lithuania within the period 2013–2015. We also aimed to compare them with previous *H. pylori* resistance rates reported in the years 2007–2008 In total 434 patients (242 adults and 192 children) from Lithuanian University of Health Sciences Kaunas Clinics and Childrens' Hospital, Affiliate of Vilnius University Hospital Santariskiu Clinics who were referred to upper gastrointestinal tract endoscopy due to dyspeptic symptoms, unclear cause anemia, abdominal pain were included in the study. Patients who had previously underwent *H. pylori* eradication therapy, had been using proton pump inhibitors (PPI), antibiotics or bismuth compounds for the last 4 weeks period were excluded from the study. During upper endoscopy two biopsies of gastral mucosa were obtained for culture of *H. pylori*. Biopsies were stored at -80°C until analysis and cultured on agar plates with 7% lysed and defibrinated horse blood. E-tests were performed for amoxicillin (MIC ≥ 0.125 mg/l), metronidazole (MIC ≥ 8 mg/l), clarithromycin (MIC ≥ 0.5), ciprofloxacin (MIC ≥ 1 mg/l), rifampicin (MIC ≥ 1 mg/l) and tetracycline (MIC ≥ 1 mg/l).

**Results:** *H. pylori* grew in 67 (28%) of 242 adult samples: resistance to clarithromycin was found in 2 (3%) cases, to metronidazole – 22 (32.8%), tetracycline - 2 (3%), ciprofloxacin - 5 (7.5%), rifampicin - 5 (7.5%). Multidrug resistant were 6 (9%) strains among adults. *H. pylori* was cultured in 94 (49%) of 192 children samples. Among children resistance to clarithromycin was determined in 33 (34%) cases, to metronidazole – 21 (21.6%) and 11 strains were multidrug resistant (11.3%). No cases of amoxicillin resistance have been detected among children and adults. Among adult patients resistance of *H. pylori* to metronidazole, clarithromycin and ciprofloxacin remained stable during 2008–2015. Meanwhile, the prevalence of clarithromycin resistance in children has increased significantly comparing previously reported 16.8% to 34% ($p < 0.05$).
**Conclusion:** There are no significant changes in the susceptibility of *H. pylori* to the most of widely used antibiotics in adults over the last years in Lithuania; however, increase in clarithromycin resistance among children seems to be dramatic. These trends might be linked with changes in national policies for treatment of pneumonia with macrolides in children.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1053 SCREENING OF PRECANCEROSIS AND EARLY GASTRIC CANCER IN NATURAL POPULATION OVER FORTY YEARS OLD, SHENGZE, CHINA: ROLE OF SERUM GASTROPANEL

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**Introduction:** Screening and early diagnosis of gastric cancer play important roles in reducing the mortality of gastric cancer.
**Aims & Methods:** The specific aims of this study were 1) to estimate the prevalence of precancerosis and early gastric cancer among natural population aged over forty in Shengze District, Jiangsu, China, 2) to identify risk factors of *H. pylori* infection and precancerous lesions, 3) to estimate the prevalence of precancerous lesions in moderate and high risk population.
**Study design:** Observational, cross-sectional.
**Methods:** 8647 residents aged over forty in 4 villages of Shengze were enrolled from 2014 to 2015. Pepsinogen I (PG I), Pepsinogen I (PG II), Gastrin-17 and serum Hp antibody were applied to screen for high risk individuels. Screened positive participants were referred to a clinical visit. Definite diagnosis was made based on endoscopic examination and histopathological test. Multivariate logistic regression was used to predict potential determinants of a definite positive diagnosis. Odds-ratios and confidence intervals were provided. Inverse probability weights generated from a propensity score model were used to adjust for non-attendance.
**Results:** Anti-Hp positive rate was 51.2%. Independent Risk factors for *H. pylori* infection were female, BMI, family member and smoking. Endoscopic information for 1300 out of the 2391 moderate and high risk individuals were obtained, representing a response rate of around 54.37%. Among them, 14 were atrophic gastritis, 233 were atrophic gastritis with intestinal metaplasia (IM), 136 were IM, and 29 were dysplasia. Remarkably, three HGIN, 2 early gastric cancer and 2 advanced gastric cancer were detected. The prevalence of gastric cancer in this region was 81/100,000. Prevalence of precancerous lesions in males was higher than that in females. The highest prevalence was found in men aged 60 to 69yr old. Risk factors identified from weighted and unweighted multiple logistic regression were smoking, Hp antibody, abnormal PG I and PGR, and G-17 level.
**Conclusion:** A relative higher overall prevalence of gastric cancer was detected in Shengze as compared to worldwide. Prevalence may be further reduced with appropriate interventions, in particular advice against the eradication of *H. pylori*.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1054 RESIDE IN A RURAL AREA AND BEING WOMAN COULD INCREASE THE RISK OF HELICOBATER PYLORI ERADICATION FAILURE, USING THE CLASSIC TRIPLE THERAPY

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**Introduction:** The rate of *Helicobacter pylori* (Hp) resistance with antibiotics treatments varies according to the geographical area. It is unknown whether factors like gender, economic level, nationality or residence place influence the therapeutic failure with the standard therapy.
**Aims & Methods:** Aim: to evaluate the influence of socioeconomic and demographics factors on the outcomes of triple therapy with omeprazole, clarithromycin and amoxicillin for 7 days (OCA-7), in *Helicobacter pylori* eradication treatment. Method: An observational and retrospective study was carried on in two health sectors from Spain (380,000 and 108,000 inhabitants respectively), between 2006 and 2010. Cases were selected using 13C-urea breath test (UBT) positive previously to first eradication treatment with OCA-7 like inclusion criteria. Patients without following eradication checking by UBT were excluded. The socioeconomic and demographics variables (gender, urban/rural residence place, nationality, and economic status) were collected using the e-medical records. Our target variable was eradication testing with negative UBT at least 4 weeks after ending OCA-7 treatment. A univariate and multivariate regression model was developed. Ethics considerations: the personal information was anonymized.
**Results:** A total of 990 UBT were obtained; of these 794 (80.2%) were positive and 604 had selection criteria. The age mean was 50 years, 55.8% of women, 21.4% lived in rural areas, most prevalent nationality was Spanish (82.8%) and 17.3% were considered as high economic level. 441 (73.4%) of the patients had a successful eradication outcome. Women were significantly associated with mayor rates of eradication failure (OR:2.03; CI 95% 1.37, 3.03) in a model of regression adjusted by age and provenance. In a second model adjusted by gender and age, live in a rural area reached a significant association (OR:1.58; CI 95% 1.01, 2.51). Age and gender adjusted Odds Ratio for eradication failure comparing middle-low economic level vs high-level was 1.10 (95% CI 0.65, 1.86), and the same one was 0.74 (95% CI: 0.41, 1.33.) for another nationality vs Spanish.
**Conclusion:** 1. Under adult population with high prevalence of *Helicobacter pylori* infection, where OCA-7 is used as eradication treatment, the probability of eradication failure is higher in women and rural areas. 2. The economic level and nationality not demonstrate to be associated in the eradication treatment failure.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1055 H.PYLORI VACA GENOTYPE IS A PREDOMINANT DETERMINANT OF IMMUNOLOGIC RESPONSE TO H. PYLORI CAGA

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**Introduction:** *H. pylori*-related peptic ulcer disease and gastric adenocarcinoma are commonly associated with cagA+ *H. pylori* strains. However, seropositivity against CagA varies among different studies with positivity below of 50%.

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Histopathology diagnosis of respondents

| Histopathology diagnosis | N | Male(%) | age(mean ± SD) | Hp(%) | Moderate risk Group(%) | High risk Group (%) |
|---|---|---|---|---|---|---|
| Chronic gastritis | 925 | 44.1 | 56.28 ± 9.50 | 56.2 | 77.98 | 37.29 |
| Atropic gastritis | 14 | 50.0 | 57.44 ± 9.73 | 64.3 | 0.99 | 0 |
| Atrophic gastritis with IM | 233 | 80.7 | 60.76 ± 9.98 | 69.1 | 16.96 | 20.90 |
| Intestinal metaplasia | 136 | 47.8 | 58.84 ± 9.81 | 70.6 | 10.61 | 10.73 |
| Hyperplastic polyp | 32 | 31.2 | 61.8 ± 11.59 | 65.6 | 2.58 | 2.82 |
| Dysplaisa | | | | | | |
| Mild | 26 | 61.5 | 61.52 ± 9.91 | 73.1 | 2.08 | 2.26 |
| Moderate | 3 | 33.3 | 70.70 ± 14.57 | 100.0 | 0.20 | 0 |
| HGIN | 3 | 66.7 | 67.00 ± 14.53 | 100.0 | 0.20 | 0.56 |
| Early gastric cancer | 2 | 50.0 | 72.50 ± 14.85 | 100.0 | 0.10 | 0.56 |
| Advanced gastric cancer | 2 | 50.0 | 72.00 ± 2.83 | 50.0 | 0.10 | 0.56 |

**Aims & Methods:** In the prospective study, we aimed to identify potential factors related to *H. pylori* CagA-immunological response specifically with focus on *H. pylori* genotype. *H. pylori* isolates, and systematically collected clinical, histological and serological data were analyzed from 99 subjects. Gastric biopsy specimens were obtained during upper GI endoscopy and were used for *H. pylori* cultivation and histological evaluation (Sydney classification). Serological profile (anti-*H. pylori*, anti-CagA) was further correlated with *H. pylori* isolates (cagA, EPIYA, vacA s/m genotype) and mucosal IL-8 mRNA expression. Subsequently, selected *H. pylori* strains were evaluated by using co-culturing model with AGS cells for CagA expression and IL-8 expression induction.
**Results:** Thirty patients (30.3%) out of total 99 microbiologically confirmed *H. pylori*-infected patients were seropositive for CagA. Seropositivity was strongly associated with the histological phenotype of gastritis, increased inflammation according to the Sydney score, IL-8 expression and cagA mRNA expression. VacA s and m polymorphisms were the major determinants for positive (vacA s1m1) or negative (vacA s2m2) anti-CagA serology that further correlated with inflammatory potential in vitro using AGS cells. In addition, in vitro co-culturing analyses confirmed functional CagA, while showing only partial correlation with CagA seropositivity, suggesting other factors as a co-determinants of the immunological response.
**Conclusion:** *H. pylori* vacA polymorphism strongly correlates with serological response to *H. pylori* cagA+ strains. Furthermore, vacA genotype was the main determinant of inflammatory potential in ex vivo and in vivo settings. The CagA-IgG positivity has a low predictive value for the infection with cagA+ *H. pylori* in a region with high vacA s1m2/s2m2 genotype prevalence.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1056 CAN BACTERIAL VIRULENCE FACTORS PREDICT ANTIBIOTIC RESISTANT HELICOBACTER PYLORI INFECTION?

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**Introduction:** Virulence factors produced by *H. pylori* contribute to the pathogenicity of the organism. Cytotoxin-associated gene A (cagA) and vacuolating-associated gene A (vacA) are the main *H. pylori* virulence factors. The frequency of virulence factor genotype differs across countries and recent data suggests that the cagA and vacA virulence factors may influence *H. pylori* treatment outcome.
**Aims & Methods:** To evaluate the impact of virulence factor genotype (vacA and cagA) on the prevalence of primary *H. pylori* antibiotic resistance. Following ethical approval and informed consent, DNA was isolated from gastric biopsies of treatment naïve adult patients infected with *H. pylori* (determined by histology) at Tallaght Hospital. Virulence factor genotyping was performed using PCR and genotypic susceptibility to clarithromycin and levofloxacin was tested using the GenoType HelicoDR assay (Hain Lifesciences). The chi-squared test was used to assess correlations between *H. pylori* genotypes and drug susceptibilities. A result was considered significant if a value of $p \leq 0.05$ was obtained.
**Results:** A total of 50 samples from *H. pylori* positive patients, average age 47.6 years, 56% male (n = 28), were analysed. 38% (n = 19) of samples possessed the cagA gene. The most common vacA genotype was the moderately virulent S1/M2 genotype at 36% (n = 18), followed by the highly virulent genotype S1/M1 at 34% (n = 17), the S2/M2 genotype at 28% (n = 14) and the S2/M1 genotype at 2% (n = 1). A clarithromycin resistant genotype was observed in 38% (n = 19) of samples. A levofloxacin resistant genotype was observed in 6% (n = 3). Resistance to both agents was found in 6% (n = 3) samples. The clarithromycin resistance rate in the $cagA^-$ group was significantly higher than in $cagA^+$ (48.3% vs 21.1%, $\chi = 3.74$, $p = 0.05$, OR 0.2844). There was no significant difference in either the clarithromycin or levofloxacin resistance rate between vacA genotypes.
**Conclusion:** $CagA^-$ and vacA S1/M2 are the dominant genotypes in *H. pylori* strains in our cohort. Infection with $cagA^-$ *H. pylori* may predict clarithromycin resistance. This may be because $cagA^+$ bacteria replicate at a higher rate and are therefore more susceptible to clarithromycin, so will be eradicated faster. Further study is planned to investigate the clinical relevance of virulence factors in *H. pylori* infection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1057 LONG-TERM CHANGES OF EXTENT OF CHRONIC ATROPHIC FUNDIC GASTRITIS AFTER H. PYLORI INFECTION OBSERVED IN AUTOFLUORESCENCE IMAGING VIDEOENDOSCOPY

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**Introduction:** Long-term infection of *H. pylori* causes subsequent changes in the gastric mucosa from inflammatory cell infiltration, glandular atrophy, intestinal metaplasia, dysplasia and cancer. Eradication of *H. pylori* improves inflammatory cell infiltration and, in part, glandular atrophy but whether areas that involved by glandular atrophy and intestinal metaplasia recover or not is unknown. Autofluorescence imaging videoendoscopy (AFI) visualize areas with chronic atrophic fundic gastritis (CAFG) including glandular atrophy and intestinal metaplasia in the gastric corpus as green mucosa in endoscopic images.
**Aims & Methods:** In this study we investigated changes of extent of CAFG after *H. pylori* eradication. Among consecutive patients with history of endoscopic treatment of early gastric cancer who visited an outpatient clinic between July 2013 and August 2014, those who received endoscopy with AFI more than two times with an interval of 2 years or longer were enrolled in this study. Patients with no evaluable AFI images of the corpus, the lesion in the corpus lesser curvature, history of gastric resection, negative and unknown *H. pylori* infection status at initial endoscopy were excluded. At least one downward and one retroflex view of AFI images of the corpus were identified for each patient. Extent of CAFG was graded by consensus of two endoscopists according to the Kimura-Takemoto classification as C-1, C-2, C-3, O-1, O-2, and O-3.
**Results:** A total of 101 patients (median age of 73 years old, 81 man and 20 women) with positive *H. pylori* infection at initial endoscopy were enrolled in this study. 43 patients received successful eradication therapy and 58 patients did not receive eradication therapy. During median (range) follow-up period of 5 (2–8) years, CAFG reduced in 9 (21%) patients in the eradication group and 7 (12%) in the non-eradication group; CAFG increased in 7 (16%) in the eradication group and 5 (9%) in the non-eradication group; and CAFG did not change in reminders (73%, 74/101) in either group (p = NS). Limitation of this study is retrospective design and inclusion of many patients with severe CAFG at initial endoscopy.
**Conclusion:** In majority of patients in this study, extent of CAFG did not improve significantly after eradication of *H. pylori*.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1058 EFFECTS OF HELICOBACTER PYLORI STATUS ON DYSPEPSIA, PEPTIC ULCER, HEALTH CARE USE OR QUALITY OF LIFE - HEP-FYN 13-YEAR FOLLOW-UP

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**Introduction:** There is evidence that eradication of *Helicobacter pylori* (Hp) improves the prognosis of the hp positve individual with dyspesia and peptic ulcer disease (PUD) (1,2).
**Aims & Methods:** The aim of this study was to evaluate the long-term effect of Hp screening in Hp positive individuals and the effect of awareness of Hp status in Hp negative individuals. The long-term effects were evaluated as the effect on dyspepsia prevalence, PUD incidence, health resource use, and quality of life in the screening group compared to the control group. This cohort study is based on the HEP-FYN study; a randomized controlled clinical trial where 20,011 individuals aged 40−65 years were invited and randomized to either Hp screening and eradication (screening group) or the control group. At baseline 12,530 were enrolled. In the screening group 1,007 individuals (17.5%) were tested positive and offered Hp eradication therapy and 4,742 were Hp negative. At the 13-year follow-up those controls, who had participated in the 5-year follow-up were invited to Hp $^{13}$C-Urea breath test. Both groups received questionnaires and additionally valid national register data were accessed for all randomized individuals.
**Results:** The Hp negative screened at baseline (aware) had a lower risk of dyspepsia at the 13-year follow-up (OR 0.78 (0.68−0.90)). However, they had a higher OR of incident PUD than controls (OR 1.88 (1.21−2.93)). No difference in dyspepsia prevalence was seen in the Hp positive. In the Hp positive cohort 11 of 876 (1.3%) individuals in the screened group and 3 out of 383 controls (0.8%) had PUD during the 13-year follow-up (OR 1.61 (0.45−5.81)). Both self-reported use of ASA/NSAID, and use of LDA and ASA/NSAID based on register data were higher in the screened group. Screening and eradication at baseline had no effect on dyspepsia related visit to GP nor did decrease use of PPI or antacids. In fact the self-reported use of ulcer drugs and antacids daily was higher and the number of endoscopies and outpatient visits were higher in the screened group in both cohorts. The SF36 mental health summary (MCS) was significantly higher in controls in both cohorts at follow-up indicating higher quality of life in controls.
**Conclusion:** The Hp negative screened at baseline (aware) had a lower risk of dyspepsia at long-term. The risk of PUD was higher in the screened group compared to the unscreened group. No health effects in favor of screening and eradication of Hp positve were observed. Selection bias due to loss of follow-up could explain the results.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1059 EFFICACY OF MULTIPLEX PCR-BASED DETECTION OF HELICOBACTER PYLORI INFECTION IN PATIENTS WITH PEPTIC ULCER BLEEDING

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**Introduction:** The diagnostic accuracy of histological and rapid urease tests (RUT) to detect *Helicobacter pylori* (*H. pylori*) infection in patients with peptic ulcer bleeding (PUB) often produce conflicting results. Multiplex PCR is a sensitive, accurate method of diagnosing *H. pylori* infection.

**Aims & Methods:** This study was conducted to assess the diagnostic values of endoscopy-based tests, such as RUT, multiplex PCR, and histology to detect *H. pylori* infection in patients with peptic ulcer bleeding. We prospectively enrolled 120 patients with gastric or duodenal ulcer diagnosed during endoscopic examination for evaluation of upper gastrointestinal bleeding. The patients were categorized into two groups according to the presence (bleeding group, $n = 53$) or absence (non-bleeding group, $n = 67$) of blood in the endoscopic finding. Prevalence of *H. pylori* infection and the sensitivity of the RUT, multiplex PCR and histology were compared.

**Results:** *H. pylori* infection was detected in 75 (62.5%) of 120 patients. The positive rates in RUT, multiplex PCR, and histology were 50.8%, 60.0%, and 36.8%. There was no significant difference in the prevalence of *H. pylori* infection between bleeding and non-bleeding group (66.0% vs. 59.7%, $p = 0.476$). The sensitivities of the RUT (71.4%) and histology (42.4%) in the bleeding group were significantly lower than RUT (90.0%) and histology (74.4%) in the non-bleeding group ($p = 0.039$ and $p = 0.006$). In the bleeding group, the sensitivity of multiplex PCR (94.3%) was significantly higher than RUT (71.4%) and histology (42.4%) ($p = 0.021$ and $p < 0.001$), and the sensitivity of multiplex PCR and RUT were not significantly different in the non-bleeding group.**Conclusion:** Recent bleeding in patients with peptic ulcer decreased the sensitivity of RUT and histology in the detection of *H. pylori* infection. In contrast, multiplex PCR was the most reliable method among the biopsy-based test to detect *H. pylori* infection in patients with peptic ulcer bleeding.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1060 CRYPT HYPERPLASTIC ENTEROPATHY IN HELICOBACTER PYLORI INFECTED IBD PATIENTS

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**Introduction:** Villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytes are histologic features of gluten-induced enteropathy, but they can be also found in other conditions. Our aim was to evaluate by validated morphometry (1) the architectural and inflammatory changes in the duodenum of patients with inflammatory bowel disease (IBD).

**Aims & Methods:** We evaluated serum samples, paraffin embedded and frozen duodenal biopsy samples from 18 IBD patients (ulcerative colitis or Crohn's disease), 13 newly diagnosed celiac disease (CD) patients and 6 controls with dyspepsia. All patients were on a gluten-containing diet. None of the IBD patients had disease specific involment of the upper gastrointestinal tract. IBD patients and controls had negative serum endomysial antibodies and did not show duodenal IgA deposits targeting transglutaminase. All patients were checked for *Helicobacter pylori* (HP) using rapid urease test during endoscopy. Paraffin embedded biopsy samples were assessed for villous height (VH), crypt depth (CrD) and villous height to crypt depth ratio (VH:CrD), while the density of CD3 and $\gamma\delta$ T cell receptor bearing intraepithelial lymphocytes (IELs) were measured in the corresponding frozen duodenal samples. The study was approved by the Ethical Committee of "Carol Davila" University of Medicine and Pharmacy, Bucharest.

**Results:** Villous atrophy with duodenal villi less than 300 μm in length was seen in 6/13 (46.15%) measurable samples of IBD patients, while crypt hyperplasia defined as over 200 μm was seen in 9/13 (69.23%). Mean VH was 316.3 μm in the IBD group, compared to 143.5 μm in the CD group and 388.3 μm in controls ($p < 0.01$). Mean CrD values were 210, 300 and 188 μm respectively ($p = 0.05$), while VH:CrD was 1.61, 0.90 and 2.14 respectively ($p = 0.03$). A subgroup analysis in the IBD patients after HP status showed a VH to CrD ratio of 1.18 in the HP positive subgroup and 1.98 in the HP negative subgroup ($p = 0.0055$). Regarding the inflammatory changes, an increased density of CD3+ IELs (>37 cells/mm epithelium) was present in 10/16 measurable samples of IBD patients (62.5%) and increased $\gamma\delta$ IELs (>4.3 cells/mm epithelium) were also present in high proportion, 13/16 (81.25%). However, mean number of CD3 and $\gamma\delta$ IELs were significantly lower in the duodenum of IBD and controls compared to CD patients (43.8, 40 and 78.8 for CD3; 7.8, 8 and 28.7 respectively for $\gamma\delta$ IELs, both $p < 0.01$). There was no difference in duodenal inflammation of IBD patients when considering subgroup analysis after HP status.

**Conclusion:** Our results show that IBD patients, when infected with HP, have morphologic changes in the duodenum similar to those seen in CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1059**

Comparison of sensitivity of diagnostic test for H.pylori between the two groups in peptic ulcer

| | Bleeding group (n = 67) | Non-bleeding group (n = 53) | p-value |
|---|---|---|---|
| RUT | | | |
| Sensitivity | 36/40 (90.0%) | 25/35 (71.4%) | 0.039 |
| Negative predictive value | 26/30 (86.7%) | 18/28 (64.3%) | 0.048 |
| Histology | | | |
| Sensitivity | 29/39 (74.4%) | 14/33 (42.4%) | 0.006 |
| Negative predictive value | 26/36 (72.2%) | 18/37 (48.6%) | 0.041 |
| Multiplex PCR | | | |
| Sensitivity | 39/40 (97.5%) | 33/35 (94.3%) | 0.596 |
| Negative predictive value | 26/27 (96.3%) | 18/20 (90.0%) | 0.387 |
| RUT/PCR concordance | 61/66 (92.4%) | 43/53 (81.1%) | 0.066 |

## P1061 EFFICACY OF 7-DAY GENOTYPIC RESISTANCE-GUIDED TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION: PROSPECTIVE TRIAL IN A HIGH-RESISTANCE SETTING

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**Introduction:** *Helicobacter pylori* (*H. pylori*) eradication rates with empirical triple therapies are rapidly declining, thus alternative treatment strategies are urgently needed. The efficacy and applicability of genotypic resistance to guide the choice of antibiotics in triple therapies have not been reported. We trialed the efficacy of a 1-week genotypic resistance-guided triple therapy in a high-resistance setting in Greece.
**Aims & Methods:** Consecutive adult patients undergoing upper endoscopy for the evaluation of gastrointestinal symptoms were prospectively assessed for inclusion. Eligible patients were those who tested positive for *H. pylori* by either rapid urease testing or histology. Gastric biopsy specimens from eligible subjects were tested with a reverse hybridization multiplex polymerase chain reaction (PCR) line probe assay (GenoTypeHelicoDR, Hain Lifescience GmbH, Germany). The 23 S rRNA gene was analyzed with three-point mutations (A2146G, A2146C, A2147G) for clarithromycin, and gyrA gene (codons 87 and 91) for fluoroquinolone susceptibility testing. A genotypic resistance-guided triple therapy was given for 7 days comprising esomeprazole (40 mg b.i.d), amoxicillin (1 gr b.i.d) and either clarithromycin (500 mg b.i.d) in the absence of 23 S rRNA mutation, levofloxacin (500 mg b.i.d) in the presence of 23 S rRNA mutation and wild type gyrA, or rifabutin (150 mg b.i.d) in presence of both 23 S and gyrA mutations. Eradication status was determined by the $^{13}$C-Urea breath test.
**Results:** Of 84 patients screened for eligibility, 28 (33.3%) were enrolled in the study (14/28 males, mean age: 56 years, non-ulcer dyspepsia: 24/28) of whom 10/28 reported a previous history of *H. pylori* treatment. All patients were *H. pylori* positive by PCR. Genotypic resistance to clarithromycin and fluoroquinolones was detected in 14/28 (naïve: 8/18, experienced: 6/10) and 4/28 (naïve: 2/18, experienced: 2/10) patients respectively. There were no cases of dual clarithromycin/fluoroquinolone resistance. All but two patients returned for eradication confirmation. The eradication rates were 92.9% (26/28) in intention-to-treat (ITT) and 100% (26/26) in per-protocol analysis. All (18/18) antibiotic-resistant *H. pylori* strains were successfully eradicated; the ITT eradication rate was 100% in patients reporting a previous *H. pylori* treatment history.
**Conclusion:** Irrespective to treatment status, a genotypic resistance-guided triple therapy, given for 7 days, achieves excellent eradication rates. Future clinical and economic evaluation data are awaited to better characterize the position of molecular susceptibility testing for *H. pylori* eradication in clinical practice
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1062 THE INVESTIGATION OF OPTIMAL H.PYLORI ERADICATION TREATMENT USING VONOPRAZAN, A NOVEL POTASSIUM-COMPETITIVE ACID BLOCKER

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**Introduction:** Vonoprazan, a novel potassium-competitive acid blocker, was reported as a component of first-line triple therapy for *Helicobacter pylori* eradication. A phase three randomized, double-blind, multicentre study in Japan revealed that the first-line eradication rate was 92.6% with vonoprazan versus 75.9% with lansoprazole.
**Aims & Methods:** The aim of this study was to investigate the relationship of patients characteristics (age, gender, renal function, degree of gastric atrophy) with success rate of *H. pylori* eradication. In our hospital, from April 2015 to March 2016, 380 *H. pylori*-positive patients with atrophic gastritis or peptic ulcer received first-line triple therapy with vonoprazan (VPZ) 20 mg in combination with amoxicillin (AMX) 750 mg plus clarithromycin (CLR) 200 or 400 mg. Ninety five patients received triple therapy with lansoprazole (LPZ) 30 mg in combination with AMX 750 mg plus CLR 200 or 400 mg in the last 3 months before using VPZ in our hospital. All treatment were administered orally twice daily for 7 days, and then followed up for an additional >4weeks and evaluated for *H. pylori* status by the C-13 urea breath test.
**Results:** The first-line eradication rate was 85.8% (326/380) in the vonoprazan group versus 55.8% (53/95) in the lansoprazole group, with the significant difference ($p < 0.01$, Chi squared test). Serum creatinine (Crn) level were measured before *H. pylori* eradication, and the median value was 0.75 mg/dl. Between Crn > 0.75 subjects and Crn < 0.75 subjects, the eradication rate was compared. In VPZ group, *H. pylori* eradication rate of Crn > 0.75 subjects was significantly higher than that of Crn < 0.75 subjects. ($p < 0.05$) In LPZ group, *H. pylori* eradication rate was not differed between Crn > 0.75 subjects and Crn < 0.75 subjects. Therefore there is a possibility that success rate of the first-line regimen including VPZ might be improved by administrating higher dose. Age, gender, and degree of gastric atrophy had no significant relation to *H. pylori* eradication rate both in VPZ and LPZ group.
**Conclusion:** Our results suggested that optimal dose of *H. pylori* eradication treatment for patients with normal renal function might be higher than that of the present vonoprazan regimen.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1063 UNSATISFACTORY EFFICACY OF LEVOFLOXACIN TRIPLE THERAPY IN THE FIRST AND SECOND LINE TREATMENT OF HELICOBACTER PYLORI INFECTION- A SYSTEMIC REVIEW AND META-ANALYSIS

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**Introduction:** Levofloxacin triple therapy has been used for the first line and second line treatment of *Helicobacter pylori* (*H. pylori*) infection for more than 10 years. Although earlier trials reported high efficacy of this therapy, recent trials show that the eradication rate of levofloxacin triple therapy were lower than 80–85%.
**Aims & Methods:** Therefore, we aimed to systemically review the efficacy of levofloxacin triple therapy in the first and second-line treatment and to assess the time trend and factors that might affect its efficacy. Prospective trials reporting the efficacy of levofloxacin triple therapy in either the first line or second line treatment of *H. pylori* infection in adults were searched from the PubMed and Cochrane database from Jan 2000 to Sep 2015. Meta-analysis was performed to calculate the cumulative eradication rate and the efficacies in subgroups.
**Results:** Of the 322 articles identified, a total of 4574 patients from 41 trials, including 16 trials in the first-line treatment and 25 trials in the second line treatment were eligible for analysis. The cumulative eradication rate was 77.3% (95% confidence intervals (CI):74.7%-79.6%) and showed a trend of decreasing efficacy with time. The eradication rate was 80.7% (95% CI 77.1%-83.7%) in the first line treatment and 74.5% (95% CI:70.9%-77.8%) in the second line treatment. The efficacies of levofloxacin triple therapy before 2008, between 2009~2011, and after 2012 were 77.4%, 79.6% and 74.8%, respectively. The eradication rate was higher when levofloxacin was given once daily (80.6%, 95% CI 77.1%-83.7%) than twice daily (73.6%, 95% CI 69.7%-77.2%). The efficacy was significantly higher in levofloxacin susceptible strains than resistant strains (81.1% vs. 36.3%, risk ratio 2.18, 95% CI 1.6–3, $p < 0.001$).
**Conclusion:** The efficacy of levofloxacin triple therapy has been lower than 80% in many countries and is not recommended when the levofloxacin resistance is higher than 10%.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1064 HELICOBACTER AND DUODENAL ULCERATION IN 2015: HOW METICULOUS ARE WE AT ASSESSING, ERADICATING AND RETESTING FOR HELICOBACTER?

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**Introduction:** The association between *Helicobacter pylori* (HP) and duodenal ulcer (DU) is well recognised. Studies have demonstrated the presence of HP in up to 95% of DU patients, with the remainder mostly related to use of non-steroidal anti-inflammatory drugs (NSAIDs). Detection of HP infection at endoscopy is commonly undertaken via the rapid urease test, however, there is a significant false negative rate in patients with an acutely bleeding DU. Thus, together with the high prevalence of HP infection in DU, some advocate empirical use of HP eradication therapy. Ulcer recurrence following successful HP eradication is low, however there is increasing evidence of antibiotic resistance, likely to cause treatment failure. Consequently, retesting to confirm HP eradication in patients with DU should be performed, a recommendation by The Scottish Intercollegiate Guidelines network (also endorsed by the British Society of Gastroenterology).
**Aims & Methods:** Aim: To identify the rate of detection and eradication of HP in patients with DU at the time of diagnosis and to determine rate of retesting to confirm HP eradication in these DU patients in real-life clinical practice.
A single centre (large north London hospital) retrospective analysis of 93 consecutive patients diagnosed with DU at upper GI endoscopy between September 2010 and September 2015. Data was obtained from the GI audit tool within the Unisoft endoscopy reporting software. Electronic patient records were used to scrutinise endoscopic HP testing, provision of eradication therapy and retesting to confirm eradication. Subgroup analysis for complicated DU was undertaken. Complicated DU was defined as symptoms of haematemesis, malaena or anaemia, or endoscopic signs of visible vessels, blood clots, a red spot, surrounding altered or fresh blood, perforation and obstruction.
**Results:** 93 patients were diagnosed with DU during the study period (age 30–98 years, M:F 1.9:1). 35% patients (n = 33) were tested for HP at endoscopy using the rapid urease test, of which 30% (n = 10) were positive. 60% of patients positive for HP received eradication therapy (n = 6). 83% (n = 77) were complicated DUs, of these 22% (n = 17) received eradication therapy. 3% patients (n = 3) were assessed for confirmation of *H. pylori* eradication. This included 2 patients with complicated DU.
**Conclusion:** From this study we conclude that the majority of patients diagnosed with DU have complicated ulcers. The testing for HP in DU patients is not routinely undertaken. More than one-third of HP-positive patients and three-quarters of complicated DU patients do not receive eradication therapy. Retesting of HP pylori following eradication therapy is extremely poor. To reduce morbidity and mortality associated with HP-related ulcer recurrence, we recommend empirical HP eradication therapy in all patients with DU, followed by retesting to confirm success in complicated DU.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1065 POTASSIUM-COMPETITIVE ACID BLOCKER–BASED THIRD-LINE TRIPLE THERAPY IN HELICOBACTER PYLORI ERADICATION AND STUDY OF THE DIVERSITY OF ANTIMICROBIAL SUSCEPTIBILITIES

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**Introduction:** The *Helicobacter pylori* (HP) eradication rate with potassium-competitive acid blocker (P-CAB)-based triple therapy is reportedly more effective than that with proton pump inhibitor (PPI)-based triple therapy for both first- and second-line treatment. However, the effectiveness of third-line eradication with P-CAB-based triple therapy has not been clarified.
**Aims & Methods:** The aim of this study was to clarify the eradication rate of P-CAB-based triple therapy and verify the antimicrobial susceptibility test using multiple strains from indivisual patients. Thirty patients were referred to our hospital for third-line therapy because of second-line eradication failure or penicillin allergy. Among them, 18 patients who underwent upper endoscopy and had a positive HP culture test result were investigated in this study. We performed biopsies from the corpus and antrum of the stomach in all patients, cultured HP, and identified 6 strains at each part (total of 12 strains per patient). The sensitivity of HP to four antimicrobial drugs (amoxicillin, clarithromycin, metronidazole [MNZ], and sitafloxacin [STFX]) was examined. After endoscopy, all patients were treated with the following third-line P-CAB-based triple therapy regimen: P-CAB 20 mg twice daily, MNZ 250 mg twice daily, and STFX 100 mg twice daily for 7 days. A urea breath test was performed after 8 weeks.
**Results:** The eradication rate of third-line triple therapy was 66.7% (12/18). The eradication rate of third-line triple therapy after second-line failure was only 53.8% (7/13). The sensitivity tests of the 12 HP strains to antimicrobial drugs revealed that all patients simultaneously had both drug-sensitive and drug-resistant strains. Additionally, the minimum inhibitory concentration of drug resistance in each strain differed even in the same patients. A four-drug-resistant strain was detected in one patient in whom third-line therapy failed. In particular, the eradication rates tended to be low in patients with STFX-resistant strains. Almost all patients with second-line failure had some MNZ-resistant strains.
**Conclusion:** P-CAB-based third-line triple therapy was less effective than conventional PPI-based triple therapy for HP eradication. Our antimicrobial resistance study indicates that MNZ-resistance might not contribute to the eradication rate associated with P-CAB-based third-line therapy. However, we found low eradication rates in patients with multidrug-resistant strains, especially STFX-resistant strains. Moreover, bacterial susceptibility to antimicrobial drugs differed among the strains colonized in the same patients. Regarding to effective eradication therapy, it is important to know the great diversity of drug-susceptibility among individual HP strains in the stomach.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1066 HELICOBACTER PYLORI SUSCEPTIBILITY TESTING IN ALBERTA, CANADA

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**Introduction:** *Helicobacter pylori* is a gram negative pleomorphic bacillus associated with gastritis, peptic ulcer disease and gastric adenocarcinomas. *H. pylori* is difficult to cultivate thus making susceptibility testing laborious. CLSI (Clinical and Laboratory Standards Institute) does not currently provide clinical breakpoints for *H. pylori*, other than for Clarithromycin, to classify strains as sensitive or resistant. It is known that resistance to antibiotics is an important cause of treatment failure. Treatment is often based on expert recommendation but rarely based on antibiogram profile. The goal of this study was to evaluate the susceptibility patterns of isolates from Edmonton and Northern Alberta patients.
**Aims & Methods:** Patients scheduled for gastroscopy underwent gastric biopsies for *H. pylori* infection. From February 2012 to October 2015, gastric biopsies were submitted in urea broth and saline. *H. pylori* was isolated from saline and antimicrobial susceptibility testing was performed by E-test (Ampicillin, Tetracycline, Metronidazole, Levofloxacin, Moxifloxacin and Clarithromycin). Interpretation of susceptibility was conducted using European Committee on antimicrobial susceptibility testing clinical breakpoints[1]. A chart review was also conducted to identify prior antimicrobial treatments.
**Results:** During the study period, 183 patients underwent gastric biopsy for *H. pylori* infection, and a total of 205 biopsies were sent for culture. The positivity rate by culture was 21% of patients (42 isolates, 39 patients). In this cohort 90% (35 patients) were previously treated for *H. pylori*. Resistance to one or more antimicrobial agent was found in 88% of positive patients (38 isolates); 33% (14 isolates) were resistant to three or more antibiotics. The majority of isolates from patients that were previously treated with Clarithromycin/ Metronidazole or triple therapy (Lansoprazole/ Amoxicillin/ Clarithromycin) were found to have resistance to Clarithromycin and Metronidazole. The rate of resistance to ampicillin 10% and tetracycline 0% was low; It was 31% for levofloxacin, 79% for Clarithromycin and 76% for Metronidazole. Overall, 64% of the isolates were resistant to Clarithromycin and Metronidazole.
**Conclusion:** This study showed the difficulties of *H. pylori* susceptibility testing due to low recovery rates of the organism from gastric biopsies. It also highlights the need for locally generated susceptibility data to better tailor therapy for each patient. Meanwhile, it also reflects the need for adequate treatment guidelines that reflect susceptibility patterns. Culture and susceptibility testing can be useful for adequate therapy for *H. pylori* eradication and antibiotic stewardship.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1067 ADDITION OF CRANBERRY TOPROTON PUMP INHIBITOR BASED TRIPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION

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**Introduction:** Proton pump inhibitor based triple therapy with two antibiotics for *Helicobacter pylori* (*H. pylori*) eradication is widely accepted, but this combination fails in a considerable number of cases. Some studies have shown that cranberry inhibit the adhesion of a wide range of microbial pathogens, including *H. pylori*. The aim was to assess the effect of cranberry on *H. pylori* eradication with a standard therapy including lansoprazole, clarithromycin and amoxicillin (LCA) in patients with peptic ulcer disease (PUD).
**Aims & Methods:** In this study, *H. pylori*-positive patients with PUD were randomized into two groupsas one by one: Group A: a 14-day LCA triple therapy with 30 mg lansoprazole bid, 1000 mg amoxicillin bid and 500 mg clarithromycin bid; Group B: a 14-day 500 mg cranberry capsules bid plus LCA triple therapy. $A^{13}C$-urea breath test was performed for eradication assessment 6 weeks after completion of the treatment.
**Results:** 200 patients (53.5% males, between 23 and 77 years, mean age $\pm$ SD: $50.29 \pm 17.79$ years) could continue treatment protocols and underwent $^{13}C$-urea breath testing. *H. pylori* eradication was achieved in 74% in Group A (LCA without cranberry) and in 89% in Group B (LCA with cranberry), ($p = 0.042$).
**Conclusion:** The addition of cranberry to LCA triple therapy for *H. pylori*, has higher rate of eradication than the standard regimen alone (up to 89% and significant).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1068 HELICOBACTER PYLORI ERADICATION EFFECT ON LIVER FAT CONTENT IN PATIENT WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction:** *Helicobacter pylori* (HP) infection role in nonalcoholic fatty liver disease (NAFLD) pathogenesis is controversial.

**Aims & Methods:** This study aimed to evaluate the effect of HP eradication on liver fat content (LFC), liver function tests (LFT), lipid profile, and homeostasis model assessment-IR (HOMA-IR) index in NAFLD. Patient with dyspepsia and increased serum levels of aminotransferases enrolled in the study. Exclusion criteria were factors affecting aminotransferases levels or HP treatment regimen. Patients with elevated aminotransferases levels and ultrasound findings of fatty liver disease were supposed for NAFLD. NAFLD liver fat score used to classify NAFLD, those with score greater than -0.64 and positive results for urea breath test (UBT), were included. Patients underwent lifestyle modifications and HP eradication. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), triglyceride (TG), cholesterol (CHOL), high and low-density lipoprotein (HDL, LDL), fasting serum glucose (FSG), LFC, and HOMA-IR were checked at baseline, after eight weeks and twenty four weeks.

**Results:** One hundred twenty patients (58 males) with the mean age of 45.39 ($\pm$9.24) were included with repeated ANOVA measurement showed a significant reduction in anthropometric measurements, laboratory parameters (except for HDL) and LFC in both groups during the study; however, no significant difference was observed between the groups.

**Conclusion:** HP eradication per se might not affect LFT, lipid profile, LFC, and insulin resistance in dyspeptic NAFLD patients

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1069 PLASMA LEVELS OF GUANYLINS ARE REDUCED IN CROHN'S PATIENTS AND IN PATIENTS WITH FAMILIAL GUCY2C DIARRHEA SYNDROME

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**Introduction:** Guanylate cyclase C (GC-C) is an intestinal receptor activated by bacterial heat-stable enterotoxins (ST), the endogenous ligands guanylin (GN) and uroguanylin (UGN) and the drug linaclotide. Familial GUCY2C diarrhea syndrome (FGDS) was diagnosed in a Norwegian family (n = 32) in 2012(1), and is caused by an activating mutation in the GUCY2C gene encoding GC-C. This activation results in increased secretion of chloride and water to the intestinal lumen, explaining the diarrhea. The patients also have an increased risk of Crohn's disease (CD, 20%). Downregulation of the GC-C pathway has previously been demonstrated in patients with IBD, including lower tissue density and gene expression of GN, which was inversely related to inflammation (2). Whether activation of GC-C affects the content of guanylins in intestinal tissue and the levels of these hormones in plasma is not known.

**Aims & Methods:** Plasma from 27 fasting patients with FGDS, 35 with CD, 24 with diarrhea- predominant Irritable Bowel Sydrome (PI-IBS-D) and 29 HC were collected and analyzed for proguanylin (ProGN) and prouroguanylin (ProUGN) using ELISA-kit (BioVendor, Karasek, Czech Republic). We performed immunhistochemistry using commercial antibodies towards GN and UGN in biopsy tissue from non-inflamed terminal ileum (FGDS n = 11, HC n = 16), and density of immunoreactive cells was quantified using computerized image analyses (3).

**Results:** Significantly lower fasting plasma levels of ProGN and ProUGN were found in FGDS and CD patients compared to the HC group ($p < 0.001$, $p = 0.013$ respectively). The plasma levels of both GN and UGN in PI-IBS patients were not significantly different from those in HC or other patient groups, ($p > 0.05$), but levels were below HC and above those observed for FGDS and CD patients. The density of GN immunoreactive cells in terminal ileum of FGDS patients was significantly higher than in HC ($P = 0.02$). Density of immunoreactive UGN cells could not be determined due to failure of UGN antibody binding. The ileal biopsies of all FGDS patients with one exception showed no signs inflammation on histological examination.

**Conclusion:** FGDS and CD patients have significantly lower plasma levels of both ProUGN and ProGN compared to HC. In FGDS patients, this finding was not associated with inflammation in the ileal mucosa nor reduced density of GN immunoreactive cells in terminal ileum, pointing to other mechanisms for the observed reduction of plasma guanylins. The increased density of GN immunoreactive cells in terminal ileum of FGDS patients may indicate impaired GN secretion from epithelial cells to plasma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1070 LOW DENSITY OF PYY IMMUNOREACTIVE CELLS IN TERMINAL ILEUM OF PATIENTS WITH FAMILIAL GUCY2C DIARRHEA SYNDROME

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**Introduction:** Familial GUCY2C diarrhea syndrome (FGDS) is a novel autosomal dominant disorder caused by an activating missense mutation in *GUCY2C*, encoding guanylate cycalse C. Activation of the guanylate cyclase C pathway, with increased formation of cellular cyclic guanosine monophosphate (cGMP), eventually results in increased secretion of chloride ions ($Cl^-$) and water into the

intestinal lumen. FGDS patients also have abnormal contractility of the small intestine, and increased risk of Crohn's disease (20%) and intestinal obstruction (25%) (1). Small intestinal hormones; namely serotonin and peptide YY (PYY) affect intestinal motility and fluid secretion. The densities of serotonin- and PYY-immunoreactive cells have shown abnormalities in other gastrointestinal disorders such as irritable bowel syndrome (2) and inflammatory bowel disorders (3).
**Aims & Methods:** The aim of the study was to investigate whether there are changes in the densities of enteroendocrine cells immunoreactive to chromogranin A (CgA), serotonin and PYY in the terminal ileum of FGDS patients compared to healthy controls. Biopsies sampled from the terminal ileum (non-inflamed mucosa) of 11 FGDS patients and 16 healthy controls were fixed in paraformaldehyde, embedded in paraffin and cut into 5 $\mu$m thinned sections. The sections were immunostained for CgA, serotonin and PYY with ultraView Universal DAB Detection Kit using the BenchMark Ultra immunohistochemistry/in situ hybridization staining module. The density of the immunoreactive cells were quantified using computerized image analysis (4).
**Results:** There was a significant lower density of PYY ($P < 0.011$), but not serotonin and CgA, immunoreactive cells in the terminal ileum of FGDS patients compared to healthy controls (Table 1).

**Table 1:** Densities of immunoreactive cells in the terminal ileum of healthy controls and FGDS patients.

Endocrine cell densities (cells/mm$^2$)

| Hormone | Control | Patient | P-value |
|---|---|---|---|
| **Chromogranin A** | $163.4 \pm 8.0$ | $164.9 \pm 24.6$ | 0.77 |
| **Serotonin** | $63.1 \pm 4.4$ | $70.0 \pm 13.4$ | 0.75 |
| **PYY** | $46.4 \pm 4.5$ | $25.3 \pm 5.8$ | $<0.011$ [a] |

Data are presented as the mean $\pm$ SEM. a: $P < 0.05$.

**Conclusion:** PYY acts as an anti-diarrheal agent by inhibiting cyclic adenosine monophosphate (cAMP) dependent agonists, and also inhibits intestinal motility. Both cGMP and cAMP activate the cystic fibrosis transmembrane regulator, and may cause diarrhea by increased secretion of $Cl^-$ and water from the enterocytes. FGDS patients have lower PYY immunoreactive cell densities than healthy controls. Further investigation of the relevance of PYY and PYY immunoreactive cell densities to the pathogenesis of FGDS is warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1071 BORONIC ACID ARRAY FOR RAPID IDENTIFICATION OF INCREASED SMALL INTESTINAL PERMEABILITY


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**Introduction:** There is need for low_cost and rapid, high-throughput tests for gut mucosal permeability. We are a multidisciplinary group of organic chemists and gastroenterology experts that is synthesizing and characterizing new chemistries for this purpose. When incorporated into organic molecules, boronic acids bind different sugars and sugar alcohols with different affinities. This variation depends on the positions where boronic acids are attached. A novel boronic acid appended viologen (BBV) sugar receptor library consisting of three synthesized BBVs (abbreviated "4,4'-o-BBV", "4,7'-o-PBBV" and "pBoB") was incorporated into a two component fluorescent assay for intestinal mucosal permeability relevant sugars (lactulose, rhamnose, 3-O-methyl-D-glucose, xylose) and sugar alcohols (mannitol, sorbitol, erythritol, galactitol).
**Aims & Methods:** The aims were to establish binding characteristics for the different permeability analytes and determine ability of the sensor library to discriminate between normal versus increased intestinal permeability (e.g., low versus high lactulose:mannitol ratios) in assay buffers and human urine. Principle component (PCA) and linear discriminant (LDA) analyses were applied to data obtained from samples spiked with known sugar concentrations and mixtures with different ratios.
**Results:** Compared to our previous work (1), twofold reductions in lower limits of detection (LLOD) and quantification (LLOQ) for lactulose were achieved with one of the BBV receptors, 4,7'-o-PBBV (LLOD 41 $\mu$M, LLOQ 72 $\mu$M). The array exhibited sharp discrimination between sugar alcohols (e.g., mannitol) and lactulose, establishing a fluorescence-based differential receptor system. It was further possible by LDA analysis to statistically segregate lactulose:mannitol ratios within a narrow range (0.1 – 0.5) that was sufficient to discern healthy versus increased small intestinal permeability. Segregation between other permutations of permeability markers was also achieved.
**Conclusion:** This proof-of-concept demonstrates that low_cost and rapid tests can be achieved using BBV sugar receptor arrays to discern normal from elevated tight junctional permeability using the most commonly used sugar and sugar alcohol markers. Flexibility to pick and choose different permutations of permeability markers for different clinical study goals or in vitro drug safety screening of large drug libraries (e.g., Caco-2, IPEC-J2, IEC-18) is not only possible, but technically and economically feasible. Because this chemistry is both rapid and reversible, it can be adapted to real-time and online monitoring of changes in permeability to multiple analytes, which is currently under development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1072 INTESTINAL PERMEABILITY IN HEALTHY FIRST DEGREE RELATIVES OF CROHN'S DISEASE PATIENTS IS ASSOCIATED WITH FUNCTIONAL CAPACITY OF MICROBIOTA


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**Introduction:** Increased intestinal permeability (IP) has been observed in a number of autoimmune diseases and may account for a susceptibility to disease triggers. We previously showed that IP in healthy subjects is not associated with the makeup of the fecal microbiota.
**Aims & Methods:** The objective of this work was to investigate if functional capacities of fecal microbiota are associated with intestinal permeability. Subjects were given a solution of two saccharide probes, lactulose and mannitol High-pressure liquid chromatography analysis of timed urine collection allows for the calculation of, the lactulose–mannitol ratio (LacMan ratio) based on the fractional excretion of lactulose divided by that of mannitol. Bacterial DNA extracted from the stool of 1098 healthy subject was sequenced for the V4 hypervariable region of the 16S rRNA using Illumina MiSeq platform. The function of the fecal microbial communities was then imputed using PICRUSt V0.1 after a rarefaction step to 30,000 sequences per sample. The PICRUSt precalculated table of gene counts based on OTUs was used to identify the gene counts in the organisms present in the stool samples. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and clusters of orthologous groups (COG) databases were used to identify gene families. Association was performed using a linear regression controlling for age, gender and smoking status. Bacterial functions with a mean count $<10$ were excluded.
**Results:** Among 3,773 KEGG and 3,618 COG functions, we found several nominal associations with IP. Using KEGG database, we found 25 associations with IP ($p < 10^{-4}$). The most significant associations involved tyrosine metabolism and degradation of aromatic compounds (K01826). Ten associations were obtain using COG database, the most significant involved in tellurite resistance (COG3615), and DNA uptake process and recombination (COG4469) ($p < 7.78 \times 10^{-4}$).
**Conclusion:** Multivariate analysis controlling for major contributing factors to IP allowed us to identify that while the specific microbial taxa do not appear to be associated with IP while microbial community functions are likely contributing to IP in healthy humans. Submitted on behalf of GEM Project research team
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1073 DYSBIOSIS AND STABILITY OVER TWO YEARS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME


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**Introduction:** There is increasing knowledge of a possible role for gut microbiota in the pathophysiology of at least subgroups of irritable bowel syndrome (IBS) patients. Fluctuations in IBS activity should be reflected by changes in gut microbiota and categorization into a status of dysbiosis or no dysbiosis if there is a causal relationship. In the present study, on defined IBS patients, dysbiosis status was studied at baseline and after two years.

**P1073**

**Table 1:** DBT = dysbiosis both times (2013 and 2015). NHD= never had dysbiosis. *Fisher's exact test. ** Abundance was measured semi-quantitatively as low, normal or high.

| | **Comparison of DBT (n = 33) vs NHD (n = 10)** Test 1 | Test 2 | **Comment** | **Agreement in abundance between test 1 and 2 (%) for DBT**** |
|---|---|---|---|---|
| | p-value | | | |
| **Bacteria** | | | | |
| Ruminococcus albus/bromii | 0.66 | 0.66 | | 76 |
| Ruminococcus gnavus | 1.00 | 1.00 | | 85 |
| Faecalibacterium prausnitzii | 0.07 | 0.24 | DBT lower at test 1 | 57 |
| Lactobacillus | 0.17 | 1.00 | | 85 |
| Streptococcus sanguinis and S. salivarius | 1.00 | 0.61 | | 85 |
| Dialister invisus | 0.73 | 0.04 | DBT higher at test 2 | 67 |
| Akkermansia muciniphilia | 0.21 | 0.66 | | 76 |
| Bacteroides fragilis | 0.45 | 0.28 | | 67 |
| Alistipes | 1.00 | 1.00 | | 82 |
| Shigella/Escherichia | 0.02 | 0.24 | DBT lower at test 1 | 52 |
| Bifidobacterium | 0.04 | 1.00 | DBT lower at test 1 | 52 |
| Bacteroides/Prevotella | 0.60 | 0.01 | DBT higher at test 2 | 61 |
| Firmicutes (Bacillli) | 0.85 | 0.86 | | 63 |
| Firmicutes (Clostridia) | 1.00 | 0.59 | | 58 |
| Proteobacteria | 0.29 | 1.00 | | 70 |

**Aims & Methods::** Sixty-three patients with IBS according to Rome III criteria were recruited to receive education about treatment options for IBS by a gastroenterologist and to be tested for dysbiosis using the GA-map$^{TM}$ Dysbiosis Test. This is a semi-quantitative 16SrRNA-based analysis of fecal bacteriae (Genetic Analysis, Oslo, Norway). The dysbiosis test was repeated two years later. Dysbiosis is defined by a dysbiosis index, DI (1–5), which is calculated by an algorithm based on the abundance and profile of bacteria. DI 3 or higher is defined as dysbiosis. The abundance of bacteria was measured as low, normal or high. All patients were seen by a gastroenterologist at the 2-year follow-up. The present abstract compares the bacterial profile in patients with dysbiosis, those without dysbiosis and any changes in dysbiosis status after two years according to the present definition of dysbiosis.
**Results:** Out of 63 IBS patients at baseline, 60 also provided stool samples after two years. Ten (17%) tested negative for dysbiosis at both rounds (never had dysbiosis=NHD), 33 (55%) had dysbiosis both times (DBT), 8 (13%) went from no dysbiosis to having it, and 9 (15%) went from dysbiosis to losing it. With focus on the first two groups: abundance of Faecalibacterium prausnitzii, Shigella/Escherichia and Bifidobacterium was significantly lower (Fisher's exact test 0.07, 0.02, 0.04) in the DBT group than the NHD group at baseline, while abundance of Dialister and Bacteroides was significantly higher in the DBT group (0.04, 0.009) after two years (Table 1). In the DBT group, the abundance of Ruminococcus gnavus, Lactobacillus, Strectococcus sanguinis and Alistipes species showed high agreement between visits 1 and 2 (82–85%), but low agreement (52–57%) for Faecalibacterium prausnitzi, Shigellea/Escherichia and Bifidobacterium species (Table 1).
**Conclusion:** Fifty-five percent of the patients had dysbiosis at baseline and after two years while 17% tested negative both times. Fifteen percent got dysbiosis and 13% lost it. Some bacteria were very stable, while others were more unstable. To test the stability may be of interest in possible future studies to treat specific disturbances in the gut microbiota.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1074 THE INFLUENCE OF PROTON PUMP INHIBITER IN HUMAN MICROBIOTA AND METABOLIC PRODUCTION RELATED TO ADVERSE EVENTS

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**Introduction:** Proton pump inhibitor (PPI) is widely used for treatment against upper GI disorders, but the attention towards its adverse effects are rarely discussed. Wallace at el. has reported that PPI exacerbates NSAID-induced small intestinal injuries in rodent models [1], and that the reduction of Bifidobacterium due to PPI treatment was related to this.
**Aims & Methods:** Our aim was to figure out how the microbiome change in human, and to analyze the difference of metabolic production after PPI use. We collected fecal samples from 21 healthy male volunteers before and after 14 days of 20 mg daily omeprazole intake. The volunteers were restricted to eat foods that would affect the microbiome. The microbiome of the fecal samples were assessed using next generation sequencing platform (Illumina MiSeq). The metabolome of same samples were also analyzed.
**Results:** Microbiome analysis showed that Actinobacteria phylum ($p = 0.016$), especially Bifidobacterium genus ($p < 0.01$) was significantly reduced after PPI use. Metabolomics analysis revealed that some of the metabolic productions increase, and some decrease significantly after PPI use.
**Conclusion:** Our results showed that the same dysbiosis occurs in human subjects as rodent models, and this suggests that PPI use may exacerbate small intestinal injuries also in human. In addition, there were also changes among the metabolic production. Further study may reveal the pathogenesis of the PPI related adverse effects.
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## P1075 PRESENCE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN PATIENTS WITH ACTIVE HELICOBACTER PYLORI INFECTION ASSESSED BY FUNCTIONAL BREATH TESTING

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**Introduction:** The aim of the present study was to investigate the presence of small intestinal bacterial overgrowth (SIBO) in patients with active *Helicobacter pylori* infection assessed by functional breath testing.
**Aims & Methods:** In total, 109 patients with gastrointestinal complaints, who were referred for the *Helicobacter pylori* $^{13}$C-urea breath test ($^{13}$C-UBT) by general practitioners and specialists, were also tested for the presence of SIBO by the glucose hydrogen ($H_2$)/methane ($CH_4$) breath test (HMBT). The Fisher's exact test was performed to compare the $^{13}$C-UBT with the glucose $H_2/CH_4$ breath test results. A detailed anamnesis was carried out about the history of *Helicobacter pylori* infection, eradication therapies, proton pump inhibitor-intake and co-morbidities.
**Results:** A total of 36/109 (33.0%) patients had a positive *Helicobacter pylori* $^{13}$C-UBT, and 35/109 (32.1%) patients had a positive glucose HMBT. Interestingly, 19/36 (52.8%) individuals with a positive $^{13}$C-UBT also had a positive glucose HMBT, whereas only 16/73 (21.9%) patients with a negative $^{13}$C-UBT showed a positive glucose HMBT ($p = 0.002$), respectively. Overall 13/38 (34.2%), 4/12 (33.3%), 1/2 (50.0%), and 1/2 (50.0%) patients, who had completed one, two, three and four eradication therapies, were diagnosed with SIBO by HMBT, respectively.
**Conclusion:** In the present study active *Helicobacter pylori* infection was found significantly associated with the presence of SIBO as determined by functional breath testing. In addition SIBO rates appeared to have increased after completed eradication therapies. However, further longitudinal studies are warranted, to fully elucidate the relationship and treatment modalities of coincident *Helicobacter pylori* infection and SIBO.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1076**
**Table 1:** Summary of results

| | Racecadotril 100mg | | Loperamide 2.0mg | | p-value |
|---|---|---|---|---|---|
| | ITT (n = 112) | PP(n = 100) | ITT (n = 111) | PP (n = 110) | |
| **Diarrhea Resolution rate (% of patients)** | | | | | |
| **25%** | 7 h | 6 h | 5 h | 5 h | ITT: 0.25 |
| **50%** | 16 h | 15 h | 17 h | 16 h | PP: 0.39 |
| **75%** | 31.5 h | 31.5 h | 32 h | 32 h | |
| **Spontaneous abdominal pain** | 80 (91%) | 77 (97%) | 80 (85%) | 79 (85%) | ITT: 0.23 PP: 0.0048* |
| **Pain on abdominal palpation** | 48 (89%) | 47 (100%) | 57 (92%) | 56 (92%) | ITT: 0.58 PP: 0.044* |
| **Abdominal distension** | 33 (88%) | 37 (100%) | 34 (87%) | 33 (87%) | ITT: 0.87 PP: 0.022* |
| **Nausea** | 49 (98%) | 47 (100%) | 34 (100%) | 33 (100%) | ITT: 0.41 |
| **Anal burning** | 25 (96%) | 24 (100%) | 25 (100%) | 24 (100%) | ITT: 0.38 |
| **Clinical success** | 97 (87%) | 94 (94%) | 88 (79%) | 88 (79%) | ITT: 0.33 PP: 0.0032* |

*Statistically significant differences All AEs were mild or moderate. The occurrence of treatment related AEs was significantly less common in the racecadotril than in the loperamide group (3.5% vs. 17%). Abdominal distension, was reported significantly more often under therapy with loperamide than with racecadotril (10% vs. 2%, p = 0.0001). Constipation did not occur in the racecadotril group, but 3 cases in the loperamide group.

## P1076 A MULTI-CENTER, RANDOMIZED, CONTROLLED TRIAL TO ASSESS THE EFFICACY, SAFETY AND TOLERABILITY OF RACECADOTRIL VERSUS LOPERAMIDE IN THE TREATMENT OF ACUTE DIARRHEA IN ADULTS

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**Introduction:** The primary endpoint was the duration of diarrhea, in hours, under the treatment of racecadotril vs. loperamide. Secondary objectives were the assessments of clinical success, diarrhea associated symptoms and adverse events.
**Aims & Methods:** A multi-center, randomized, single-blind study in adult Chinese outpatients, aged between 18 and 70, with acute diarrhea was conducted according to GCP, relevant national guidelines and the Declaration of Helsinki. Patients received racecadotril 100 mg tid p.o. or loperamide 2.0 mg tid p.o. until recovery (defined as 12 hours with no stools or 2 consecutive normal stools) or for a maximum of 3 days. Clinical success was defined as complete resolution of all symptoms of acute diarrhea. The occurrence of constipation was defined as no stools during 36 or more consecutive hours after diarrhea resolution.
**Results:** A total of 223 patients were entered into the study. Among 13 withdrawals, 4 patients were lost to follow-up and 9 patients were protocol violators (poor medication compliance, no exact time to resolution of diarrhea despite resolution of diarrhea).
Diarrhoea resolved rapidly with both racecadotril and loperamide. Analysis of the per protocol population showed a significantly greater reduction of spontaneous abdominal pain, pain on abdominal palpation and abdominal distension with racecadotril. As for the resolution of nausea, anal burning and anorexia, both treatments were similar to each other and of no significant difference. Clinical success was significantly higher in the per protocol analysis favoring the patients being treated with racecadotril (table 1).
**Conclusion:** Both medications were rapidly effective in the treatment of acute diarrhea in adults. In terms of time to resolution of diarrhea, they were similar to each other and no significant differences were demonstrated. However, a significantly higher clinical success rate was achieved with racecadotril than with loperamide. With racecadotril abdominal symptoms, typically associated with diarrhea, resolved more effectively and a lower occurrence of AEs was observed, especially for abdominal distension and constipation.
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H. Weigmann: Employee of Boehringer Ingelheim Pharma GmbH&Co.KG
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## P1077 A RAPID POINT-OF-CARE TEST (POCT) IN ADULT CASE-FINDING IN PRIMARY CARE FOR COELIAC DISEASE: A COST-EFFECTIVENESS STUDY

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**Introduction:** Celiac disease (CD) is under diagnosed. Primary care physicians can play an active role in the finding of patients with CD using simple tools such as a POCT based on the detection of deamidated gliadin peptide antibodies (DGP). This test has previously shown to have similar sensitivity and specificity as standard serologic analysis of antibodies to tissue transglutaminase (ATTG) (1).
**Aims & Methods:** Aim: 1. To assess the effectiveness of a strategy of adult case-finding in primary care for CD in terms of new diagnosis compared with the same period of previous year; 2. To evaluate if this strategy was cost-effective. Methods: Case finding in a primary care setting by testing for CD by using the POCT (Simtomax) in subjects with predefined signs and symptoms or belonging to at-risk groups. Inclusion criteria: Age >14 years, to be on a gluten containing diet. Exclusion criteria: testing for antiendomysial (AEA) and ATTG during the previous year and previous diagnosis of CD. POCT was performed simultaneously with coeliac serology (AEA and ATTG). Duodenal biopsies for histology and gammadelta cells (by flow cytometry) were obtained if POCT and/or ATTG were positive. Sensitivity (S), specificity (E), PPV and NPV were assessed. Cost-effectiveness of diagnostic strategies using serology or POCT was compared.
**Results:** We included 350 patients (76% women; age 42 ± 1). The POCT was positive in 29 (8.2%). Of these, ATTG was positive in 3/29 (2 Marsh 3, 1 Marsh 1). Of the 26 with POCT+ and ATTG- the histology showed 1 Marsh 3 (AEA- and increase gammadelta). S of POCT for CD was 100% (40–100), E 93% (89–95), PPV 14% (4.5–33), NPV 100% (98.5–100). Prevalence of CD was 1.1% (4/350; 95%CI, 0.3–3.4), doubling the observed in the previous year. POCT followed by duodenal biopsy if positive was the most cost-effective approach (serology, 13724€/case of CD detected; POCT, 7600€/case of CD detected; using the NHS tariffs).
**Conclusion:** The high NPV of POCT allows ruling out CD in primary care. The prevalence of CD using a case-finding strategy was three times higher than in the general adult population in Catalonia. POCT was the most cost-effective approach in routine clinical practice in primary care.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1078 POTENTIAL COELIAC DISEASE OF THE ADULTS: TO TREAT OR NOT TO TREAT, THAT IS THE QUESTION!

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**Introduction:** Potential coeliac disease (PCD) of adults still remains an almost unexplored area.
**Aims & Methods:** 1) to explore the prognostic role of Marsh grade (0 vs 1) in adult PCD patients; 2) to evaluate the effects of a gluten containing diet (GCD) in asymptomatic PCD patients. We prospectively enrolled all consecutive adult PCD patients diagnosed at our tertiary center, who completed a 6-year follow-up period. According with Marsh grade they were divided into Group 0, comprising subjects with Marsh 0 and Group 1, including Marsh 1-patients. Symptomatic patients started gluten free diet (GFD), while asymptomatic subjects were kept on GCD and were followed-up to evaluate serological and clinical features, development of villous atrophy and immune-mediated disorders (IMD).
**Results:** 56 PCD patients were enrolled (21 [37.5%] in Group 0 and 34 [62.5%] in Group 1). Forty-three patients were symptomatic (15 in the Group 0 and 28 in the Group 1, P = NS) and started GFD. Among them, 8 (28.5%) in Group 1 developed IMD during the follow-up, but none patient in Group 0 (P = 0.03; OR = 4.2 [95% IC 0.5–37.5]). The remaining 13 asymptomatic PCD patients kept on GCD. During the follow-up, 69% developed CD-related symptoms, 46% became atrophic and 61% developed IMD, without significant differences between the two groups. Interestingly, confronting patients kept on GCD with

those on GFD, we found that the first ones had a higher risk of developing IMD than patients on GFD (61% vs 18%, P = 0.03, OR = 3.3 [95% IC 1.04–10.5]).
**Conclusion:** Although PCD with normal mucosa seems to be a milder disease, GCD leads to a high risk of developing atrophy, and, especially, a significant risk in developing IMD than patients on GFD. Adult PCD patients should early start GFD despite symptoms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1079 MAY MUCOSAL TRANSCRIPTOMIC ANALYSIS PREDICT THE DEVELOPMENT OF GLUTEN-RELATED DISORDERS AMONG MICROSCOPIC ENTERITIS?

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**Introduction:** To evaluate: i. mucosal baseline mRNA expression of tissue transglutaminase 2 (tTG2), interferon gamma (IFN$\gamma$), Toll-like receptor 2 (TLR2) and Myeloid differentiation factor 88 (MyD88) in patients with microscopic enteritis (ME), ii. their predictive value for the diagnosis of underlying disorder in a 2-year follow-up, iii. and their accuracy in discriminating the development of celiac disease (CD) and gluten sensitivity (GS).
**Aims & Methods:** We retrospectively enrolled 89 patients with ME of different etiology, which was defined within a 2-year follow-up. Baseline histological examination had been performed on Hematoxylin–Eosin stained sections and immunohistochemistry of CD3 had been used for intraepithelial lymphocyte count (IELs). ME was defined according to the criteria of Bucharest Consensus Conference. For each patient, formalin-embedded biopsy samples of the duodenum referred to the period of ME diagnosis were retrieved. Real-time polymerase chain reaction (RT-PCR) was used to detect the amount of mRNA coding for tTG2, IFN$\gamma$, TLR2 and MyD88. Control group was represented by duodenal healthy specimens from 15 dyspeptic subjects. Comparisons among continuous variables were performed by One way analysis of variance (ANOVA) and Bonferroni's test. The $\chi 2$ test was used for categorical variables. Pearson's test was used to evaluate correlations. Receiver operating curves (ROC) were drawn for all four markers to estimate sensitivity and specificity in discriminating the development of CD and GS.
**Results:** After a mean period of follow up of $21.7 \pm 11.7$ months, the following diagnoses were achieved: gluten related disorders in 48 subjects (31 CD; 17 GS) and non-gluten related ones in 41 (29 Irritable Bowel Syndrome – IBS; 12 Others). CD patients had the highest tTG2 levels ($8.3 \pm 4.5$) compared to GS ($3.6 \pm 2.7$), IBS ($3.5 \pm 1.8$), other ME ($5.3 \pm 2.3$) and negative controls ($1.001 \pm 0.089$). The ANOVA plus Bonferroni analysis showed that CD > Other ME > GS=IBS > negative controls. A cut off of 2.258 was able to discriminate between CD and GS with a sensitivity of 52.94% and a specificity of 87.1%. CD patients had the highest IFN$\gamma$ levels ($8.5 \pm 4.1$) compared to GS ($3.3 \pm 2.8$), IBS ($3.3 \pm 2.6$), other ME ($4.6 \pm 2.1$) and negative controls ($1.001 \pm 0.15$), with CD > Other ME > GS=IBS > negative controls. A cut off of 1.853 was able to differentiate CD and GS with a sensitivity of 47.06% and a specificity of 96.77%. Patients with non gluten-related causes of ME exhibited the highest TLR2 levels ($6.1 \pm 1.9$), greater than GS ($3.1 \pm 1.8$), IBS ($3.5 \pm 2.0$), CD ($4.1 \pm 2.4$) and negative controls ($1.006 \pm 0.18$), with Other ME > CD=GS=IBS > negative controls. TLR2 were unable to predict the development of CD or GS. Patients with CD expressed MyD88 levels similar to non gluten-related causes of DL ($7.8 \pm 4.9$ and $6.7 \pm 2.9$), higher than GS ($4.2 \pm 2.3$), IBS ($4.3 \pm 2.4$), and negative controls ($0.99 \pm 0.17$), thus CD=Other DL > GS=IBS > negative controls. A cut off of 3.722 was able to differentiate CD and GS with a sensitivity of 52.94% and a specificity of 74.19%.
**Conclusion:** Our results suggest that a single marker is unable able to predict a discrimination among ME underlying conditions as well as between CD and GS. Mucosal transcriptomic levels of tTG and IFN$\gamma$ may predict the development of CD more than GS with high specificity, despite an expected low sensitivity. TLR2 do not discriminate the development of CD from GS. MyD88 show that intestinal permeability is more marked increased when a severe intestinal damage underlies ME.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1080 FLOW CYTOMETRIC ANALYSIS OF ABERRANT INTRA-EPITHELIAL LYMPHOCYTES IN REFRACTORY COELIAC DISEASE

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**Introduction:** Coeliac disease (CD) is a chronic gluten dependent enteropathy characterized by an increased mortality, mainly due to its complications: refractory coeliac disease (RCD), ulcerative jejunitis and enteropathy associated T-cell lymphoma (EATL). These complications share a common origin as suggested by aberrant intraepithelial T-lymphocytes (IELs) (CD3-, CD45+, CD103+, CD7+, CD4-, CD8-, cytCD3+) [1]. In the last years flow cytometry (FC) analysis of duodenal IELs emerged as the best tool to identify this aberrant monoclonal T-cell population [2]. It was also shown that a percentage of aberrant IELs > 20% predicts evolution of RCD into overt EATL [3].
**Aims & Methods:** To evaluate the reproducibility of the FC analysis of IELs. To see if high levels of aberrant IELs (> 20%) can predict development of EATL and mortality in Italian patients with RCD. From February 2012 to March 2016 IELs were isolated from 26 duodenal biopsies of 13 patients affected by RCD (9F, age at complication $54 \pm 13$ years; follow-up from complication median 44 months, 12–55, 25°-75°) and immunophenotyped using FC. In 7 patients FC was repeated in different times during follow-up. Patients were divided into two groups according to the percentage of aberrant IELs (cut off value > 20%). Survival and development of EATL were then assessed in the two groups.
**Results:** In the 7 patients in whom FC was repeated more than once almost identical results of the immunophenotype of IELs were obtained, suggesting a stability of the IELs phenotype. Increased aberrant IELs (> 20%) were found in 5/13 RCD patients and 3 of them died (2 EATL, 1 RCD type 2). In the group without increased aberrant IELs (< 20%) no patients died (median follow-up 44.5 months, 35.25–67.25, 25°-75°), but one patient developed an EATL.
**Conclusion:** FC is a reproducible tool in the diagnostic workout of RCD patients. We confirm that high levels of aberrant IELs (> 20%) increase the risk of poor outcomes in RCD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1081 LONG-TERM RECOVERY OF HEALTH STATUS OF PATIENTS WITH CELIAC DISEASE

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**Introduction:** The symptomatic celiac disease has important biological and psychosocial consequences due to their impact on patient's expectations, habits and health-related quality of life. The introduction of gluten-free diet improves biological changes, symptoms and quality of life of celiac disease patients. Despite its beneficial effect, maintenance of the gluten-free diet also has a negative impact on the life of celiac disease patients due to the restrictions, difficulties in diet follow-up and additional economic costs. We do not know how quality of life changes over time with gluten-free diet.
**Aims & Methods:** Our aim was to determine if celiac disease patient's quality of life remains stable during the follow-up of gluten-free diet. Methods: Prospective observational study in a cohort of celiac disease patients diagnosed by positive serology and duodenal biopsy, with good clinical and serological response to gluten-free diet. Quality of life was evaluated by administering the generic questionnaire EuroQol-5D. In a sub-group of patients, the specific questionnaire CD-QOL was also administered. Patients were visited twice, at entry in the study and after 12 months. In a group of patients, results were compared with those of the EuroQol-5D administered 10 years before, with the disease already treated.
**Results:** Sixty-five patients, with a median age of 40 years and 6 years of evolution since diagnosis were included. Twenty-one also completed the CD-QOL and in another11 EuroQol-5D was compared with that obtained 10 years before. According to the Morisky scale, complete adherence to diet was referred by 86% of patients. The perception of quality of life remained stable, with a median score of the visual analogue scale basal and after 12 months of 80 vs 80 (p = ns). The median tariff of the EuroQol-5D also persisted unchanged (0.87 vs 1.0 after 12 months, p = ns). The median global score of the CD-QOL also persisted unchanged during the year of follow-up (79 vs 76, p = ns). Results of the EuroQol-5D obtained 10 years before also were similar (VAS 83 and tariff 0.87, p = ns).
**Conclusion:** The quality of life of celiac disease patients on gluten-free diet remains stable during long term follow-up.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1082 DENTAL ENAMEL DEFECTS, DENTAL CARIES, ORAL LICHEN PLANUS IN PATIENTS WITH CELIAC DISEASE - PROSPECTIVE COHORT STUDY INTRODUCTION:

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**Introduction:** Celiac disease (CD) can be associated with various oral manifestations. No large study clarifying the exact relation and role of gluten-free diet (GFD) on these manifestations. We prospectively studied these objectives in large cohort of patients.
**Aims & Methods:** Total of 264 CD patients were enrolled for 1 year in tertiary care referral hospital along with controls (n = 269). History of oral lesions was taken and dental examination was done. Enamel defects were classified as to Aine classification. After institution of gluten-free diet (GFD), patients were followed for 3 year.

**Results:** CD patients had significantly more enamel defects. Enamel defects were more common in patients with mixed dentition as compared to permanent dentition. Dental caries were similar in frequency in celiac patients as compared to controls. Oral lichen planus was more common in celiac patients. After institution of GFD at three-year follow up, no significant improvement occurred in enamel defects but improvement in oral lesions was seen.
**Conclusion:** This study proves the association of CD with dental enamel defects in childhood. After 3 year of GFD, improvement occurred in lichen planus. Hence, CD should be added to differential diagnosis of dental enamel defects, lichen planus. All physicians and dentists must be aware of these associations. The diagnosis of celiac disease can sometimes be made from a smile.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1083 CELIAC DISEASE WITH NEGATIVE HLA-DQ2.5/8 IN SPAIN: SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** More than 90% of celiacs carry the heterodimer HLA-DQ2.5. The DQ8 heterodimer is commonly observed in DQ2.5 negative celiacs. Only a small number of celiacs are DQ2.5/8 negative, many of whom encode half of DQ2.5 heterodimer. The European genetic cluster on celiac disease (CD) showed that 6% of celiacs were DQ2.5/8 negative (93% of them encoded half of DQ2.5 heterodimer) (1).
**Aims & Methods:** To perform a meta-analysis of the presence of negative HLA-DQ2.5/8 CD in Spain.
Studies evaluating the HLA-DQ2.5/8 profile in CD patients in Spain were included. Bibliographies until March 2016 were searched. Inclusion criteria were: 1.Diagnosis of CD with villous atrophy using ESPGHAN criteria; 2. Full description of DQ2.5/8 haplotypes. Studies with duplicated data were excluded. Frequency of negative genetic celiac study was determined. Meta-analyses were performed using the inverse-variance method. A random effects model was used when heterogeneity (I2 statistic) was present. An $I2 > 76\%$ was considered as considerable heterogeneity.
**Results:** The electronic search retrieved a total of 199 publications, from which 44 were selected for a more thorough revision. Finally, 14 studies were included, which comprise 3167 patients with CD. The overall frequency of negative HLA-DQ2.5/8 was 3% (95% CI, 2–4; 2963 patients; $I^2$ 81%), after excluding 2 outlier studies, with doubts about genotyping was correct. Remaining heterogeneity was due to only one study, after excluding it $I^2$ was 36% without changing the overall frequency. Among 105 negative DQ2.5/8 CD patients, the presence of half of the DQ2.5 heterodimer was observed in 80 (55 DQB1+ and 25 DQA1+; in 5 was not described) (80/100, 80%; $p = 0.022$ vs the European study). Thus, at least 20 out of the 105 patients had both alleles of DQ2.5 negative. The overall frequency of being negative for the two alleles of DQ2.5 and for DQ8 was 1% (95% CI, 0–1; 2450 patients; $I^2$ 28%).
**Conclusion:** In Spain, 3% of celiacs are DQ2.5/8 negative. The frequency of CD with the two alleles of HLA-DQ2.5 and DQ8 negative is higher in Spain than in the European study.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1084 SERUM ANTI-GANGLIOSIDE M1 ANTIBODIES AND NEURON-SPECIFIC ENOLASE LEVELS IN NEUROLOGICAL ASYMPTOMATIC CELIAC DISEASE PATIENTS – PILOT STUDY

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**Introduction:** Celiac disease is a multisystemic, autoimmune disorder, triggered by gluten ingestion, occurring in genetically predisposed patients. Clinical outcome includes several extraintestinal manifestations with neurologic ones. Neurologic complications are observed in about 10% of patients but previous studies confirmed presence of subclinical changes of autonomic nervous system activity. Aetiology of neurologic involvement in celiac disease is complex and not fully explored. Presence of anti-ganglioside antibodies have been described in the serum of celiac patients with peripheral neuropathy and cerebellar ataxia. Neuron-specific enolase is a marker of autonomic nervous system and its increased levels has been described in several disorders.
**Aims & Methods:** Aim of the study was to evaluate the anti-ganglioside M1 antibodies and neuro-specific enolase serum concentrations in neurological asymptomatic celiac patients and its correlation with activity of disease and duration. 34 celiac patients (70% females, mean age 34 years, $41.2 \pm 16.6$) without neurological symptoms and 34 healthy volunteers (mean age 34 years, $35.8 \pm 9.5$) were tested for the anti-ganglioside M1 antibodies and for neuron-specific enolase concentrations in serum by ELISA.
**Results:** In celiac patients mean level of anti-ganglioside M1 antibodies was significantly higher in comparison to control, group ($1.59 \pm 1.07$ vs $.83 \pm .67$, $p < .001$, Mann-Whitney test). The neuron-specific enolase serum concentration was not significantly higher in celiac group (5.2vs 3.76, $p = .659$, Mann-Whitney test). In celiac group neuron-specific enolase level and anti-ganglioside M1 antibodies level did not correlate with age (respectively $R = -.02$, $p = .926$, and $R = .15$, $p = .422$, Spearman's rank).
**Conclusion:** Presence of anti-ganglioside M1 antibodies in neurologic asymptomatic celiac patients might be the marker of development of subclinical changes in nervous system. Further investigations are needed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1085 PREVALENCE OF CELIAC DISEASE IN PATIENTS WITH AUTOIMMUNE THYROID DISEASE – A META-ANALYSIS

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**Introduction:** Several screening studies have indicated an increased prevalence of celiac disease (CD) among individuals with autoimmune thyroid disease (ATD) but estimates have varied substantially.
**Aims & Methods:** The aim of this study was to examine the prevalence of CD in patients with ATD. A systematic review of articles published in PubMed Medline or EMBASE until September 2015 was done. Non-English papers with English-language abstracts were also included, as were research abstracts without full text available when relevant data were included in the abstract. Search terms included "celiac disease" combined with "hypothyroidism" or "hyperthyroidism" or "thyroid disease". Fixed-effects inverse variance-weighted models were used. Meta-regression was used to examine heterogeneity in subgroups.
**Results:** A pooled analysis, based on 6,024 ATD patients, found a prevalence of biopsy-confirmed CD of 1.6% (95% CI = 1.3–1.9%). Heterogeneity was large ($I^2 = 70.7\%$). The prevalence was higher in children with ATD (6.2%; 95%CI = 4.0–8.4%), than in adults (2.7%) or in studies examining both adults and children (1.0%). CD was also more prevalent in hyperthyroidism (2.6%; 95%CI = 0.7–4.4%) than in hypothyroidism (1.4%; 95%CI = 1.0–1.9%).
**Conclusion:** About 1 in 62 patients with ATD have biopsy-verified CD. We argue that patients with ATD should be screened for CD given this increased prevalence.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1086 SERUM ANGIOPOIETIN-2 IS AN ACCURATE CAPSULE ENDOSCOPY SCREENING TOOL FOR THE DETECTION OF SMALL BOWEL ANGIODYSPLASIA

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**Introduction:** Small bowel angiodysplasia (SBA) accounts for 50% of cases of obscure gastrointestinal bleeding (OGIB). SBAs bleed recurrently with a proportion of patients dependent on red cell transfusions and a significantly impaired quality of life. Although treatment options are limited, an early diagnosis and directed therapy can significantly improve outcome. CE is the most sensitive diagnostic tool for SBA, however the indication for CE not only includes OGIB, but Iron Deficiency Anaemia (IDA), suspected small bowel

Crohn's disease, malabsorption etc, placing a large demand on the service. Due to the varied presentation of SBA and intermittent nature of bleeding it can be difficult to clinically prioritise patients for CE. We have previously presented an association between SBA and serum alterations in Ang1, Ang2 and TNF$\alpha$ levels, however it is unknown whether these angiogenic factors are driven by bleeding overall or whether they are specific for SBA.

**Aims & Methods:** To determine whether alterations in serum angiogenic factors are specific for SBA, and whether they could be used as screening tools to prioritise patients for CE. Blood samples were prospectively collected from all patients undergoing CE for the investigation of OGIB and IDA at our Hospital over a 12 month period. Haemoglobin (Hb) level and renal function were measured in the hospital laboratory and serum samples were stored at $-80^{\circ}$C for batch analysis. Levels of Ang1, Ang2 and TNF$\alpha$ in serum were measured using commercially available ELISA kits. Based on CE reports patients were divided into 3 groups–SBA, other abnormalities, and normal small bowel. Results of each factor were expressed as a mean/median and compared between groups, and analysed for association with clinical factors using a Mann Whitney U test. The potential for serum Ang1/Ang2 as a CE screening tool was explored using Receiver Operator Characteristic (ROC) curve analysis.

**Results:** A total of 120 patients were included; 53% (n = 64) Male, with a mean age of 63 years. Hb levels were lower in patients with positive findings than in the normal group (11.2 g/dL vs 12.3 g/dL, $p < 0.02$). Levels of each factor are outlined in Table 1. In keeping with our previous findings patients with SBA have significantly elevated serum levels of Ang2 compared to non-SBA patients, with a trend towards lower levels of Ang1 and TNF$\alpha$. In addition, serum Ang2 levels even when controlled for anaemia and chronic kidney disease were selectively elevated in patients with SBA. As a CE screening tool for SBA, we established a cutoff Ang2 level of 2600 pg/ml, giving a sensitivity of 84% and negative predictive value of 87%. Although the positive predictive value for SBA was only 50%, of these false positives; 50% had significant findings (including enteritis, polyps and a small bowel tumour) which would warrant an expedited CE, making the true false positive rate only 26%. Although the Ang1/Ang2 ratio was also specific for SBA over other conditions, the ROC was similar to that of Ang2 alone, conferring no additional benefit to the need for the use of 2 markers.

| | SBA n = 40 Mean age = 73 Mean Hb = 11.2 | Abnormal n = 40 Mean age = 60 Mean Hb = 11.3 | Normal n = 40 Mean age = 55 Mean Hb = 12.7 |
|---|---|---|---|
| **Ang1(pg/ml)**Median P value compared to SBA | 40976 | 44770 0.33 | 47639 0.04 |
| **Ang2(pg/ml)**Median P value compared to SBA | 3759 | 2261 < 0.004 | 2620 < 0.003 |
| **TNF$\alpha$(pg/ml)**Median P value compared to SBA | 5.76 | 9.76 0.12 | 10.14 0.13 |

**Conclusion:** Serum Ang2 levels are specifically elevated in patients with SBA compared to other causes of OGIB. In our cohort a cutoff level of 2600 pg/ml would be an effective CE screening test at initial referral to prioritise patients likely to have SBA and other significant findings, with an earlier diagnosis potentially directing treatment and improving outcome.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1087 CROHN'S DISEASE DIAGNOSED BY CHANCE IN PATIENTS SUBJECTED TO CAPSULE ENDOSCOPY FOR THE INVESTIGATION OF OBSCURE GASTROINTESTINAL BLEEDING

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**Introduction:** According to the European Society of Gastrointestinal Endoscopy guidelines, small bowel capsule endoscopy (SBCE) is the method of choice for the investigation of suspected Crohn's disease (CD), in patients with a non-diagnostic initial ileocolonoscopy. Our aim was to compare the number of cases with findings suggestive of CD amongst patients subjected to SBCE for the investigation of obscure gastrointestinal bleeding (OGIB) and compare this figure with the number of cases subjected to SBCE for suspected CD.

**Aims & Methods:** Retrospective analysis of data collected prospectively between March 2003 and December 2015. During this period, 3025 patients were subjected to SBCE in our Department for the investigation of a) OGIB (n = 1396, 46.1%), b) suspected small intestinal CD (n = 552, 18.2%), because of abdominal pain and/or chronic diarrhoea, positive inflammation markers, but a negative upper GI endoscopy and ileocolonoscopy and a negative history of aspirin and/or non steroid anti-inflammatory drugs intake, and c) proximal small bowel involvement in patients with known CD (n = 411, 13.6%)

**Results:** Among the 552 patients subjected to SBCE because of suspected CD, lesions suggestive of CD (apthoid or deep ulcers with focal or diffuse inflammation of the jejunal and/or ileal mucosa) were seen in 211 (38.2%) patients [139 (25.2%) patients with chronic diarrhoea and 72 (13.0%) patients with abdominal pain respectively]. Notably, the ileocaecal valve had not been intubated in 52 (24.6%) of the 211 patients. Among the 1396 patients investigated for OGIB, lesions suggestive of CD were seen in 209 (14.9%) and again in 71/209 (33.9%) the ileocaecal valve had not been intubated during the preceding colonoscopy. Focusing on the group of patients with unexplored terminal ileum during the preceding ileocolonoscopy and lesions suggestive of CD at SBCE, there was a statistically significant difference between those with OGIB over patients with suspected CD (p = 0.03). Because most of the patients included in the study were referred to our Department only for SBCE, we cannot estimate the proportion of patients with OGIB and lesions suggestive of CD in whom the diagnosis of CD was finally confirmed by prospective follow-up.

**Conclusion:** In a substantial number of patients subjected to SBCE for the investigation of OGIB, lesions suggestive of CD are seen by chance, in the absence of clinical suspicion for CD. This is especially true in patients in whom the terminal ileum has not been investigated during the preceding colonoscopy. Although the clinical significance of these findings is not known, a meticulous follow-up of these patients is deemed mandatory.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1088 REBLEEDING RATE AFTER ENDOSCOPIC TREATMENT OF SMALL BOWEL ANGIODYSPLASIAS WITH SINGLE-BALLOON ENTEROSCOPY: PREVALENCE AND RISK FACTORS

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**Introduction:** Small bowel angiodysplasias are the most common cause of obscure gastrointestinal bleeding in the Western world. Safety and efficacy of short-term endoscopic treatment with argon plasma coagulation (APC) have been demonstrated, but data on the long-term effectiveness of this procedure are still scarce.

**Aims & Methods:** We aimed to evaluate the rebleeding rate after endoscopic treatment of small bowel angiodysplasias with single-balloon enteroscopy and analyse potential risk factors for rebleeding. Between 2010 and 2015, all consecutive patients who were treated with single-balloon enteroscopy with APC due to small bowel angiodyspalsias were included. Rebleeding was defined as recurrence of obscure gastrointestinal bleeding or a decrease in haemoglobin $\geq$ 2 g / dL. Risk factors for rebleeding were analysed.

**Results:** Thirty-one patients were included, 76.5% male, with a mean age of 69.1 $\pm$ 15.8 years. Rebleeding rate after a median follow-up time of 25.0 (IQR 12.1–36.5) months was 35.5% (11/31). Among patients with rebleeding, 36.4% (4/11) had obscure GI bleeding and 63.6% (7/11) a haemoglobin decrease $\geq$ 2 g/dL. Among those patients with recurrent bleeding, 1 or 2 additional endoscopic treatment sessions successfully controlled rebleeding in 81.8% (9/11) of patients. Treatment with oral anticoagulants was the only factor significantly associated with increased risk of rebleeding (57.1% versus 17.6% in patients without anticoagulation, p = 0.028).

**Conclusion:** After a median follow-up of 25.0 months, the rebleeding rate after endoscopic treatment of small bowel angiodysplasias with single-balloon enteroscopy with APC was 35.5%. Patients under treatment with oral anticoagulants had the higher risk of rebleeding.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1089 EXRESS VIEW READING EFFICIENTLY REDUCES READING TIME FOR SMALL BOWEL CAPSULE ENDOSCOPY: A PROSPECTIVE MULTICENTRIC STUDY

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**Introduction:** Reading capsule endoscopy films is a time-consuming exercise and reducing the reading time is of high priority for gastroenterologists. Beside the Medtronic capsule, no express reading algorithm has been validated prospectively at the present time. We report a prospective evaluation of an "express view" reading mode for Intromedic° capsule system.

**Aims & Methods:** On hundred patients with occult or overt gastrointestinal bleeding were prospectively included after negative bidirectional endoscopy at ten participating centers. All patients had a capsule endoscopy (Medtronic°, Seoul) examination of the small bowel and the films were read in normal mode, a second reading was performed in express view mode in a second center. For each lesion, the precise location, nature and relevance were collected. Discordant results between the 2 readings will be reviewed by an expert board to confirm discordance or reclassify into concordant cases. We report results of the first 36 cases. Complete data of the series will be presented at the congress.

**Results:** Thirty-six patients from 4 centers (mean age 64.5 yrs) had a capsule endoscopy. Table1 shows the diagnostic yield, transit time measurement and evaluated transit times at both normal and express view reading. Both modes allowed a high diagnostic yield. Discordance (lesion relevance, type of lesion,

presence of lesion) between the 2 readings occurred in 17 cases and corresponded mostly to different interpretations of the same lesions.

| | Normal reading | Express view |
|---|---|---|
| Pts with possible small bowel diagnosis (%) | 21 (58%) | 22 (61%) |
| P2 lesions nb (nb / % pts) | 26 (13 / 36%) | 15 (12 / 33%) |
| Mean reading time | 34.6 min (14–90) | 18.5 min (4–40) |
| Gastric transit time (mean) | 71.6 min | 58.4 min |
| Small bowel transit time (mean) | 218.2 min | 191.9 min |

**Conclusion:** Express view reading allows an important shortening of Intromedic° capule film reading with a high diagnostic yield. Discrepancies between 2 capsule readings are usual and require expert checking to clarify the exact sensitivity and specificity of the 2 modes of reading. Express view may represent a satisfying new informatic algorithm to reduce capsule endoscopy reading time.
**Disclosure of Interest:** J.C. Saurin: Fees for consulting: Medtronic, Intromedic, Capsovision
All other authors have declared no conflicts of interest.

## P1090 POSTPRANDIAL FLOW MEASUREMENTS OF THE MESENTERIC ARTERIES AND PORTAL VEIN USING MAGNETIC RESONANCE IMAGING: A PILOT STUDY

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**Introduction:** Patients with chronic gastro intestinal ischemia (CGI) suffer from severe postprandial abdominal pain due to insufficient postprandial increase of mesenteric blood flow, usually caused by atherosclerotic stenosis of the supplying gastrointestinal arteries. The diagnosis of CGI remains challenging as chronic abdominal pain due to other causes is common and stenosis of the mesenteric arteries are often asymptomatic due to extensive collateral circulation. Hence, a reliable non-invasive test to assess the hemodynamics of the mesenteric vessels is needed. In cardiovascular radiology, cardiac blood flow is measured using Magnetic Resonance (MR) imaging. This technique has not yet been explored to quantify intestinal blood flow.
**Aims & Methods:** We aimed to determine the feasibility of flow measurements using MR imaging to assess the hemodynamics of the mesenteric arteries and portal vein and establish a set of reference values under fasting and feeding conditions in healthy volunteers. Therefore, healthy volunteers underwent MR flow measurements of the abdominal aorta at a level just above the celiac trunk (AA), the celiac artery (CA), superior mesenteric artery (SMA), and portal vein (PV) on a 1.5 Tesla MR scanner during both inspiration and expiration. An ECG-gated, velocity-encoded cine gradient-echo sequence was used to measure blood flow using a 32-channels surface coil. First, we performed MR flow measurements in fasting state. Consecutively, blood flow was assessed 10, 20, 30 and 40 minutes after oral intake of 400 mL (600 kcal) nutritional drink.
**Results:** Nine healthy volunteers aged $\geq$ 50 years (3 male) underwent MR flow measurements. Median blood flow in mL/stroke of the AA, PV and SMA increased significantly postprandially compared to baseline, both during expiration (AA 47.0 vs. 58.2, $p = 0.028$; PV 24.3 vs. 40.3, $p = 0.008$; SMA 4.9 vs. 13.2, $p = 0.011$) and inspiration (AA 38.2 vs. 47.6, $p = 0.046$; PV 21.6 vs. 33.3, $p = 0.008$; SMA 3.4 vs. 14.3, $p = 0.021$). Blood flow of the CA also increased postprandially, both during expiration and inspiration, but these results were not statistically significant. See table. The relative increase in blood flow was most prominent in the SMA (expiration 169%, inspiration 321%) and these values at baseline and maximal postprandial flow overlap completely during both inspiration and expiration.

Median and IQR of MR flow measurements in mL/stroke of abdominal aorta (AA), portal vein (PV), celiac artery (CA) and superior mesenteric artery (SMA) before (0 minutes) versus after nutritional drink at maximal postprandial flow (max flow). * P-value $<0.05$ is considered significant

| | T = 0 median (IQR) | T max flow (min) | Max flow median (IQR) | p-value |
|---|---|---|---|---|
| **AA expiration** | 47.0 (40.3–53.4) | 30 | 58.2 (47.0–80.1) | 0.028* |
| **AA inspiration** | 38.2 (28.6–43.9) | 20 | 47.6 (37.1–55.7) | 0.046* |
| **CA expiration** | 10.1 (7.0–13.0) | 10 | 11.0 (7.3–16.4) | 0.374 |

(continued)

Continued

Median and IQR of MR flow measurements in mL/stroke of abdominal aorta (AA), portal vein (PV), celiac artery (CA) and superior mesenteric artery (SMA) before (0 minutes) versus after nutritional drink at maximal postprandial flow (max flow). * P-value $<0.05$ is considered significant

| | T = 0 median (IQR) | T max flow (min) | Max flow median (IQR) | p-value |
|---|---|---|---|---|
| **CA inspiration** | 7.7 (6.5–13.2) | 40 | 9.0 (3.8–11.1) | 0.086 |
| **SMA expiration** | 4.9 (3.2–5.7) | 40 | 13.2 (11.0–14.2) | 0.011* |
| **SMA inspiration** | 3.4 (1.1–6.9) | 30 | 14.3 (7.5–17.3) | 0.021* |
| **PV expiration** | 24.3 (21.5–26.6) | 20 | 40.3 (30.0–48.2) | 0.008* |
| **PV inspiration** | 21.6 (20.8–30.1) | 30 | 33.3 (28.5–41.2) | 0.008* |

**Conclusion:** It is feasible to non-invasively assess the hemodynamics of the mesenteric arteries and portal vein using MR flow measurements. We have established a set of reference values under fasting and feeding conditions. Further research is needed for the applicability of this technique in the diagnostic work-up of CGI, starting with pre- and postprandial MR flow measurements in patients with CGI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1091 A PROSPECTIVE, QUANTITATIVE ASSESSMENT OF PAIN AND QUALITY OF LIFE BEFORE AND 3 AND 12 MONTHS AFTER VASCULAR TREATMENT FOR CHRONIC MESENTERIC ISCHEMIA

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**Introduction:** There are no prospective data on pain or health-related quality of life (HRQOL) in patients treated for chronic mesenteric ischemia (CMI). This prospective study was designed to determine the change of pain intensity and HRQOL in CMI patients treated for atherosclerosis or celiac artery compression.
**Aims & Methods:** Patients with CMI treated with percutaneous mesenteric artery stenting or retroperitoneal endoscopic release of the arcuate ligament in celiac artery compression syndrome between August and December 2013 were enrolled. For pain we used the visual analogue scale for pain intensity (VAS-PI, graded 0–100 mm). We assessed overall pain, postprandial pain and pain after exercise in the preceding week. We also assessed the number of pain free days, and use of analgetics for abdominal pain. For HRQOL we used the 36-item Short Form Health Survey (SF-36). All parameters were obtained before (baseline; BL) and at three (FU3) and twelve months (FU12) after the intervention.
**Results:** Thirty patients were included, 80% female, mean age 57 (range 20–90) years. Diagnoses were single vessel (n = 8) and multi-vessel intraluminal atherosclerotic stenoses or occlusions (n = 15), and celiac artery compression (n = 7). The VAS-overall pain improved from median 60 (IQR 48–72) at BL to 2 (IQR 0–4) at FU3 and 10 (IQR 0–40) at FU12, $p < 0.0001$. At these time-points the postprandial VAS improved from 74 (IQR 67–84) to 2 (IQR 0–40) and 10 (IQR 0–48), $p < 0.0001$. The VAS-pain after exercise improved from 65 (IQR 50–80), to 4 (0–20) and 10 (IQR 0–35), $p < 0.0001$. Analgetic use for abdominal pain decreased from 74% to 17% and 19% of patients ($p < 0.009$), the number of pain free days per week increased from median 0.9 (IQR 0–2) to 6 (IQR 1–7) at FU3 and 7 (IQR 0–7) at FU12, $p < 0.0001$. In all cases the difference between BL and FU3 and F12 was highly significant, but no significant difference between FU3 and FU12 was seen. Of the three diagnosis groups the differences showed similar significant improvements from BL to FU3 and FU12 for single- and multivessel atherosclerosis, but not for CACS patients. The HRQOL measured with SF-36 improved for five of eight dimensions (role physical, bodily pain, vitality, social functioning and mental health) and the both (physical and mental) component summary scores.
**Conclusion:** This prospective study showed marked pain reduction after 3 and 12 months, associated with improved quality of life. The magnitude of change underscores the potential benefit CMI patients may experience from restore of the mesenteric artery inflow.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 09:00–17:00
**NUTRITION II – POSTER EXHIBITION**

## P1092 LACTOBACILLUS AND BIFIDOBACTERIUM PROBIOTIC STRAINS REDUCE CHOLESTEROL LEVELS AND AFFECT THE GUT MICROBIOTA IN OBESE MICE

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**Introduction:** Obesity is a widespread problem, is considered to be an inflammatory condition. Probiotic strains could modify inflammation and recently were hypothesized to be effective to treat obesity. Our recent studies have demonstrated the ability of previously selected and characterized Lactobacillus delbrueckii subsp. bulgaricus IMV B-7281, L. casei IMV B-7280, Bifidobacterium animalis VKB and B. animalis VKL strains to assimilate cholesterol in vitro [1] and to normalize microbiota spectrum in cases of Staphylococcus infection [2].
**Aims & Methods:** The aim was to study the influence of Lactobacillus and Bifidobacterium probiotic strains on cholesterol levels in serum and the gut microbiota on mouse obesity model. Experimental studies were conducted on female BALB / c mice aged 6–8 weeks (17–24 g). For modeling obesity mice during 21 days were receiving a high-calories diet (HCD); after 22 days, these mice started to receive usual diet and L. delbrueckii subsp. bulgaricus IMV B-7281, L. casei IMV B-7280, B. animalis VKL, B. animalis VKB (each strain separately) or compositions B. animalis VKB / B. animalis VKL (in the ratio 1: 1) or B. animalis VKB / B. animalis VKL / L. casei IMV B-7280 (at 1: 1: 2 ratio). The probiotic strains were suspended in sterilized saline. Mice were treated with these strains and compositions at a dose of 1 x $10^6$ cells daily to the animal orally during 7 days. We organized 7 groups of BALB/c mice (12 mice in each group), that include 2 control groups (intact mice that received normal diet (control 1) and HCD-treated mice (control 2)) and 5 groups of mice that received HDC and probiotic strains in monocultures or their compositions. Body weight was measured once a week. Blood samples and feces were taken on the 7, 15 and 21$^{st}$ days from HCD start and on the 4, 9, 15, 21 and 30$^{th}$ days from the beginning of probiotic strains introduction.
**Results:** We established that 3 weeks of HCD diet leads to an increasing of body weight in mice up to $6.8 \pm 0.3$ g and free cholesterol level in the blood serum from $4.82 \pm 0.36$ to $12.33 \pm 0.77$ and also leads to significant changes of gut microbiota spectrum (increased the number of gram-positive cocci - staphylococci, streptococci, and microscopic fungi, but reduced the number of Lactobacillus spp., Bifidobacterium spp.). Under the influence of all probiotic bacteria and compositions we observed decreasing the level of serum cholesterol from the 4$^{th}$ day of treatment in mice receiving HCD, but under the influence of L. casei IMV B-7280 and L. delbrueckii subsp. bulgaricus IMV B-7281 in monoculture and L. casei IMV B-7280 / B. animalis VKB / B. animalis composition we observed a complete normalization of cholesterol level on the 9$^{th}$, 15$^{th}$ and 21$^{st}$ day respectively. Thus, L. casei IMV B-7280 demonstrated most effective hypocholesterolemic activity, dramatically reducing the level of serum cholesterol even compared with the levels in intact mice. After strains and compositions entering to HDC-treated mice a we observed gradual normalization of body weight, the most ($5.8 \pm 0.6$ g) in the group of mice treated with L. casei IMV B-7280. Treatment with all strains and compositions reduced the total amount of gram-positive bacteria and microscopic fungi in the intestinal contents, but significantly increased the number of Lactobacillus spp., Bifidobacterium spp. and coliform bacteria.
**Conclusion:** L. delbrueckii subsp. bulgaricus IMV B-7281, L. casei IMV B-7280, B. animalis VKB and B. animalis VKL in monoculture and in the various compositions are promising to create probiotic preparations for the prevention and treatment of metabolic diseases, which progress is accompanied by violation of cholesterol metabolism and gut microbiota spectrum.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1093 INTRAGASTRIC BALLOON: A COMPARATIVE STUDY ADJUSTABLE TWELVE MONTHS BALLOON VERSUS CONVENTIONAL SIX MONTHS BALLOON


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**Introduction:** The conventional Intragastric Balloon (IGB) for usage within up to 06 months has been used for more than 25 years in more than 80 countries, as an aid for weight loss. More recently, an adjustable intragastric balloon has been approved for usage within up to 12 months. That brought us a questioning on which procedure should be recommended and in what situations each one should be applied.
**Aims & Methods:** This study compares the usage of two types of liquid balloons available in Brazil, analyzing which of them offer better conditions for weight loss, with a lesser incidence of complications and intercurrences. Data were collected among 868 patients of 05 different private centers, 695 made use of the 06 months conventional balloon and 173 made use of the 12 months adjustable balloon. Study period took place between January 2015 and March 2016. We have analyzed the mean weight loss on both types of balloon during the study period, also the BMI variation, the percent EWL (Excess Weight Loss), the percent of early removals and incidence of ulcers, as well as other intercurrences, which were divided by period of time, considering each type of balloon. Data were analyzed using Student t-test, and andTukey post-test. The level of significance was set at $p < 0.05$.
**Results:** Usage of 06 months balloon has shown results very similar to results with a 12 months balloon, regarding weight loss. The mean Percent EWL was more than -59.10% (±39.32%) [6 months] versus 59.61% (±33.45%) [12 months]. Mean weight loss was -18.57 kg (±8.33 kg) [6 months] versus -20.54 kg (±10.27 kg) [12 months]. Mean variation of BMI was -4.91 kg/m$^2$ (±2.91 kg/m$^2$) [6 months] versus -5.68 kg/m$^2$ (±3.48 kg/m$^2$) [12months]. Removal due to initial intolerance was little higher with the 06 months balloon than with the 12 months balloon (2.7% 6 months balloon versus 1.8% 12 months balloon). Nonetheless, regarding intercurrences and complications, the 12 months balloon presented a higher incidence of gastric perforation (0.6% versus 0.1%), bleeding due to Dieulafoy lesion (0.6% versus 0.1%) and ulcers (16.8% versus 0.3%). The appearance of ulcers was higher from the sixth month of balloon usage (61.1%) and the most used approach was changing the balloon or a dose increase of IBP (89.7%). In 10.3% of ulcer cases, the IGB removal was necessary.
**Conclusion:** The 06 months Intragastric Balloon has presented similar results concerning weight loss and BMI variation when compared to the 12 months Adjustable Intragastric Balloon, however, with the latter, the incidence of ulcers, bleedings and gastric perforation is higher than with the conventional 06 months balloon.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1094 EXERCISE DIFFERENTIALLY CHANGES METABOLIC DYSREGULATION AND GUT MICROBIOTA IN DIFFERENT DIETS


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**Introduction:** Exercise improves metabolic dysregulation. However, the roles of exercise on gut microbiota have seldom been investigated.
**Aims & Methods:** We conducted an in vivo study to examine how exercise influences metabolic dysregulation and gut microbiota in different diets. C57BL6 mice were divided into four groups: normal diet without exercise (NS group, N = 6), normal diet with exercise (NE group, N = 4), high fat diet without exercise (HS group, N = 6) and high-fat diet with exercise (HE group, N = 4). Body weight, blood sugar, and glucose tolerance tests were compared. The differential DNA expression levels of Bacteroides spp. and Firmicutes spp. in stool specimens were analyzed by using quantitative polymerase chain reaction.
**Results:** After 16 weeks of experiment, body weight gain was significantly greater in high fat diet groups than normal diet groups. Body weight gains between the exercise and non-exercise groups were not significantly different. HE group showed a greater improvement in the glucose tolerance ability ($92.5 \pm 15.2$ mg/dL) compared with the HS group ($165 \pm 28.3$ mg/dL) ($P < 0.05$). In the stool specimens, we found that exercise significantly increased the amount of Bacteroides spp, especially in the NE group (NE: $6.70 \pm 4.86$; HE: $2.43 \pm 0.96$; NS: $2.29 \pm 0.96$; HS: $0.81 \pm 0.49$, $P < 0.01$). On the contrary, increased amount of Firmicutes spp. was observed in the stool specimens of HS group (NE: $0.50 \pm 0.75$; HE: $0.46 \pm 0.17$; NS: $0.51 \pm 0.24$; HS $1.51 \pm 0.68$, $P < 0.01$).
**Conclusion:** Exercise improves glucose tolerance ability in mice with high fat diet. In addition, the gut microbiota was changed with increased Bacteroides spp. by exercise in both diet groups, especially in the normal diet group.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1095 CD24 KO MALE MICE AS A MODEL SYSTEM OF EARLY ONSET OBESITY IN MEN WITH INSULIN HYPER-SENSITIVITY

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**Introduction:** The heat stable (HSA)/CD24gene encodes for a heavily-glycosylated cell surface protein.The role of CD24in carcinogenesis is being extensively investigated. Its role in diabetes and obesity is not clear.PPAR$\gamma$ is a regulator of adipogenesis that plays a role in insulin sensitivity, lipid metabolism, and adipokineexpression.
**Aims & Methods:** Aim: To assess gender-dependent changes in CD24/HSA KO mice fed with normal and high-fat diet (HFD). Methods: Body weight (BW), water and food consumption were closely monitored from birth in HSA+/+ ($N > 120$) andHSA-/- ($N > 120$) mice for one year. The experiment was repeated twice. Insulin (0.5 IU/kg) sensitivity and glucose (1 gr/kg) tolerance was determine thrice. Adipose tissuefrom kidney (KF), testicular (TF), and liver (LF) were isolated from KO and WT mice. High-throughput sequencing of stool 16S rRNA genes was assessed in the enteric microbial populations of the KO and WT mice, male and female, normal and HFD consumers. $N = 10$ in each group. Taxa analysiswas performed on the core taxa prevalent in more than >25% of samples. Extraction of vascular fraction from adiposetissues was performed and primary cultures of adipocytes were established. Fecal transplantation was used todetermine whether sensitivity to insulin or weight gain is dependent on the murine gut microbiota.
**Results:** Water and food consumption was similar for the KO and WT mice in normal andHFD. Mean BWof the KO was higher than that of their WT littermates, particularly in males and surprisinglywith greater insulin sensitivity (10–20%) and glucose uptake (30%). It remained valid for mice fed with HFD. No suchdifferences were observed among females. Significant differences in BW, KF, TFand LF were demonstrated between CD24 KO and WT mice. Aadipocytes size of the KO ($8258 \pm 2359$ uM2) was significantly higher thanthat of the WT ($5471 \pm 2030$ uM2) mice ($P < 3.51$ E-09) (Fig.3). PPAR$\gamma$ expression was higher (x1.5) in CD24 KO mice. Enteric bacterial populations were significantly different between KO and WT mice (normal diet) by unweighted ($R = 0.32$, $P < 0.01$) $\beta$-diversity analysis. These differences became more apparent when mice were kept on HFD by weighted ($R = 0.43$, $P < 0.01$) and un-weighed $\beta$-diversity analysis ($R = 0.31$, $P < 0.01$) as well as by specific bacterial taxa (Fig.4). Moreover, when the wt male mice were systemically treated with anti-CD24 mAbs, the phenotype of the KOmice was restored to that of the KO mice.
**Conclusion:** 1. CD24 negatively regulate PPAR$\gamma$ expression in male. 2. The association between CD24 and insulinsensitivity, and the oncogenic potential of CD24, suggest a possible mechanism for diabetes as a cancer risk factor. 3. CD24KO male mice may serve as a model of male early obesity and insulin sensitivity. 4. mAb to CD24 can be used in diabetic patients as they improve insulin sensitivity.
**Disclosure of Interest:** N. Arber: Consultation Fee: Bio-view, Check-cap, Bayer Stock Shareholder: Micromedic, Gi-view
All other authors have declared no conflicts of interest.

## P1096 A RANDOMIZED CROSS-OVER STUDY ON THE EFFECTS OF FODMAPS ON GASTRIC ACCOMMODATION, SYMPTOM GENERATION AND EMOTION IN HEALTH AND IRRITABLE BOWEL SYNDROME

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**Introduction:** There is accumulating evidence for the benefit of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) in the management of irritable bowel syndrome (IBS) symptoms. Whether FODMAPs alter the gastric accommodation (GA) response to nutrients, and whether this contributes to symptom generation and induces changes in emotion, remains to be assessed.
**Aims & Methods:** The objectives were to assess the impact of different FODMAPs on the intragastric pressure (IGP) response to nutrient ingestion (which reflects GA), symptom generation and on emotions. A high resolution manometry and infusion catheter were positioned in the proximal stomach of healthy volunteers (HV) and IBS patients. After a stabilization period of at least 10 minutes and when the participant was in a late phase II of the hunger cycle, a FODMAP or control solution (fructans and glucose, respectively) was intragastrically infused at 60 mL/min until maximal satiation (0–5 scale), three days to one week apart in a single-blind randomised cross-over order. Questionnaires on gastrointestinal symptoms and mood and emotion were collected before infusion and then every 15 minutes up to 3 hours. Positive and negative affect were assessed before infusion, immediately after infusion and then every hour up to 3 hours after infusion. IGP data were presented as change from baseline, whereas symptom and psychological scores were presented as absolute score (mean ± SEM). Data were analysed using linear mixed models and repeated measures ANOVA.
**Results:** Twenty healthy volunteers (19–32 y, 10 men, 18–44 BMI) and 19 IBS patients (18–55 y, 4 men, 18–32 BMI) were included. Nutrient volume tolerance did not differ significantly within groups. However, although not significant, IBS patients had a lower nutrient volume tolerance compared to healthy controls (fructans: $p = 0.059$, glucose: $p > 0.05$). GA was significantly inhibited in HV following fructan infusion compared to glucose ($p = 0.002$) and significantly higher in IBS compared to HV for both solutions (fructans: $p = 0.012$, glucose: $p = 0.021$). Regarding gastrointestinal symptoms, fructans induced significantly more flatulence and cramps in IBS compared to HV ($p = 0.026$ and $p = 0.015$, respectively). Throughout the study, fructans were associated with significantly higher fatigue scores in IBS patients ($p < 0.010$). In addition, tension scores were significantly higher in IBS ($p < 0.002$), whereas the feeling of being in control was significantly lower in the patient population ($p < 001$), both for fructans and glucose. Finally, IBS patients reported higher scores for negative affect throughout the study compared to HV ($p < 0.035$).
**Conclusion:** IBS patients have a differential IGP response compared to HV. In addition, these results confirm that FODMAPs are involved in symptom generation in IBS patients and show that IBS patients are characterized by a more negative psychological state in comparison with HV. Unraveling the sensory, neural and/or hormonal pathways involved in the differences in gastric physiology requires further mechanistic studies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1097 THE FEATURES OF POSTPRANDIAL ABDOMINAL HEMODYNAMICS IN PATIENTS WITH VISCEROPTOSIS

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**Introduction:** Abdominal circulation has important physiological significance, providing nutriment and function of the digestive system, maintaining nutritional hemostasis.
**Aims & Methods:** Aim: to study features of abdominal hemodynamics in patients with visceroptosis. Materials and methods. The study included 69 patients (mean age $22.28 \pm 3.7$ years) with visceroptosis and 52 patients without visceroptosis (control group). Patients are matched by sex and age. Exclusion criteria: presence of operations on digestive organs in history, medication affecting ciculation.Patients underwent doppler ultrasound common hepatic artery, splenic artery, superior mesenteric artery, portal vein fasting and 30 minutes after food sample standardized by protein (14 g), fat (10 g) (45 g).
**Results:** It was not detected when assessing abdominal blood fasting differences in hemodynamic parameters.In carrying out food samples in the postprandial period in patients with visceroptosis recorded lower volumetric flow rate for all vessels: the portal for vene1124.0 [1030.0–1419.0] ml / min against 1373.0 [1136.0–1567.5] ml / min in the control group ($U = 433.5$; $Z = -2.1$; $p = 0.0342$) at the common hepatic arteri 341.0 [295.0–394.0] ml / min vs. 412 in the comparison group, 0 [331.0–521.0] mL / min ($U = 335.0$; $Z = -2.3$; $p = 0.0218$) at the splenic artery 396.0 [292.0–538.0] ml / min versus the comparison group at 502.0 [394.0–594.0] mL / min ($U = 328.0$; $Z = -2.1$; $p = 0.0399$), in superior mesenteric artery 988.0 [837.0–1272.0] mL / min versus 1136.5 in the comparison group [992.0–1465.0] mL / min ($U = 1625.5$; $Z = -2.2$; $p = 0.0314$). blood flow changes correlated with the degree of visceroptosis: for portal vein from any ptosis ($rs = -0.21$; $p < 0.05$), according to the common hepatic artery from gastroptosis ($rs = -0.38$; $p < 0.05$) by the superior mesenteric artery from kolonoptosis ($rs = -0.86$; $p < 0.05$) and peripheral vascular resistance: on the common hepatic artery ($rs = -0.46$; $p < 0.05$); by splenic artery ($rs = -0.33$; $p < 0.05$), the superior mesenteric artery ($rs = -0.79$; $p < 0.05$).
**Conclusion:** Patients with visceroptosis in postprandial low blood flow volume is recorded for abdominal aortic vessels. The factor that determines a lower volumetric flow rate is the length of the mesenteric vessels, undergoing the greatest changes during ptosis. Food sample reveals a latent deficiency of blood flow in patients with visceroptosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1098 EFFECTIVENESS OF BETA-CRYPTOXANTHIN FOR NONALCOHOLIC STEATOHEPATITIS

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**Introduction:** We previously reported that in nonalcoholic steatohepatitis (NASH) patients there was an excess intake of carbohydrates/energy and low intakes of protein/energy, polyunsaturated fatty acid and zinc. We also reported that a two-year interventional diet, consisting of 30–35 kcal/kg of ideal body weight, 55% of carbohydrate/energy, 20% of protein/energy, 1.0–2.0 of ratio of polyunsaturated to saturated fatty acid, and sufficient amounts of vitamins and zinc, would be effective for improving anthropometric and biological parameters in NASH patients. There have been a few reports in

NASH patients about effectiveness of carotenoids, especially beta-cryptoxanthin (b-crypt).
**Aims & Methods:** In this study, we clarified intake and serum concentration levels of b-crypt in NASH patients, and conducted a clinical trial to assess whether b-crypt would inhibit the progression of NASH. A priori approval for the study was obtained from the Ehime University Hospital Research Ethics Board and UMIN Clinical Trials Registry. All subjects provided written informed consent.
**Results:** Intake and serum levels of b-crypt were significantly lower in NASH patients (n = 30) than in nonalcoholic fatty liver (NAFL) patients (n = 30) and healthy controls (n = 15). We randomly assigned NAFLD patients to receive the trial beverage containing 3 mg of b-crypt (n = 20) or placebo (n = 20) beverage for 12 weeks. In both NASH and NAFL patients, serum GGT levels were significantly reduced with b-crypt therapy, as compared with placebo. Serum oxidative LDL and interleukin (IL)-6 levels were significantly decreased and serum SOD and IL-10 levels were significantly increased in both NASH and NAFL patients who received b-crypt therapy. We also randomly assigned NASH patients to receive the trial beverage containing 3 mg of b-crypt, 12 mg of Zn and 30 mg of a-tocopherol enriched beverage (n = 20) or only 3 mg of b-crypt enriched beverage (n = 20). Both trial beverages had same effects.
**Conclusion:** These data suggest that b-crypt therapy may be effective for improving anti-oxidant and anti-inflammation in NASH patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1099 A RANDOMIZED PATIENT -BLIND CONTROLLED PHASE III STUDY TO COMPARE THE EFFICACY AND SAFETY OF INTRAVENOUS FERRIC CARBOXYMALTOSE (FERINJECT®) WITH PLACEBO IN PATIENTS WITH ACUTE ISOVOLEMIC ANEMIA AFTER GASTRECTOMY

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**Introduction:** Acute isovolemic anaemia is a decreased haemoglobin (Hb) concentration with normal or even increased blood volume after gastric cancer surgery. Unfortunately this condition is largely overlooked, undiagnosed and under-treated which may negatively influence both short and long-term outcomes. We therefore assessed if intravenous iron used in the postoperative setting may efficiently correct anaemia and confer clinical benefits in this population.
**Aims & Methods:** This randomized controlled trial was conducted in 7 centres across Korea to evaluate the efficacy and safety of FCM in treating of acute isovolemic anaemia post gastrectomy. The study group was administered FCM (1.000 mg for body weight ≥50 kg or 500 mg iron if <50 kg). The placebo group received 0.9% normal saline (200 mL for bodyweight ≥50 kg or 100 mL if <50 kg). Pts with a serum ferritin level of <15 ng/mL and Hb-level <10 g/dl at week 3 received an additional dose of 500 mg iron or 100 mL normal saline. The primary endpoint was the number of responders at 12 weeks. Secondary endpoints included Hb and iron parameter evolution, percentage of patients requiring alternative anaemia management and the safety of FCM. Quality of life (QoL) was assessed using the EORTC QLQ-C30 and STO22 questionnaires at 3 and 12 weeks. Pts were blinded to treatment throughout the study to minimise bias.
**Results:** 430 gastric cancer pts with Hb 7 to <10 g/dl at 5–7 postoperative days after oncologic resection were assessed for efficacy. At baseline, the mean Hb concentration was 9 and 9.2 g/dL for the FCM and placebo arms respectively. At end of study, 92% of pts receiving treatment with FCM achieved a Hb increase of at least 2 g/dL or Hb > 11 g/dL versus 54% in the placebo arm (p = 0.001). Significant correction of anaemia and iron parameters in favour of FCM was observed at all time points (Table 1). The estimated blood loss for each group was 187 and 192 mL (FCM and placebo; p = 717). Alternative anaemia management was required in 4 pts in the study group and 18 patients in the placebo group (1.8% vs. 7.1%; p = 0.006). QoL improvements were observed for the global quality of life, fatigue and dyspnoea components of the EORTC QLQ C30 questionnaire. FCM was well tolerated with no severe, serious or anaphylactic reactions reported.

**Table 1:** Laboratory Parameters

| Time-point & Parameter | FCM | Placebo | p-value |
|---|---|---|---|
| **Baseline** | | | |
| Hb (g/dL) | 9 | 9.2 | 0.010 |
| serum ferritin (ng/mL) | 115.9 | 137.1 | 0.094 |
| TSAT (%) | 10.8 | 10.5 | 0.662 |
| **3 week** | | | |
| Hb (g/dL) | 11.6 | 10.6 | 0.001 |
| serum ferritin (ng/mL) | 508.8 | 75.6 | 0.001 |
| TSAT (%) | 29.8 | 13.9 | 0.001 |
| Hb ≥ 10 g/dL | 210(96.8) | 155(71.1) | 0.001 |
| Hb ≥ 11 g/dL | 165(76.0) | 90(41.3) | |

**Conclusion:** Administration of FCM for managing acute isovolemic anaemia post gastrectomy is effective in correcting anaemia and iron deficiency with minimal toxicity profile. The treatment also appears to be beneficial for patients, especially in relation to fatigue and dyspnoea.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1100 CONVENTIONAL CONTINUOUS INSULIN INFUSION THERAPY OF PERIOPERATIVE MANAGEMENT AFTER ESOPHAGECTOMY

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**Introduction:** In diabetes patients of esophagectomy is high rate morbidity (anastomotic leakage and infection) because of insulin resistance, hyperglycemia and surgical diabetes. On the other hand, intensive or conventional insulin therapy was controversial. Variability of blood glucose and severe hypoglycemia was influenced the mortality in ICU patients.
**Aims & Methods:** To evaluate the influence of diabetes on perioperative complication with conventional continuous insulin infusion therapy after esophagectomy.
Patients and Methods: 1. A total 64 cases (Sep 2013–July 2014) were underwent esophagectomy. About hyperglycemia more than 180 mg/dl, we started continuous insulin infusion therapy and managed blood glucose between 110–150 mg/dl. 2. We retrospectively discussed factors affecting morbidity of perioperative complications after esophagectomy in diabetes.
**Results:** 1. Among 64 patients, 27 (42%) patients (Group HG) used continuous insulin infusion therapy for hyperglycemia (180 mg/dl). 37(58%) patients (Group NG) did not use insulin. 2. Group HG patients had no increased risk for morbidity compared with Group NG. Rate of perioperative complications were Clavien-Dindo classification IIIb: HG: NG 18% vs. 22%, leakage: 10% vs. 8.3%, infectious disease: 46% vs. 38%. 3. Compared with patients with comorbidities, those with ≥2 comorbidities including diabetes had a statistically significance for anastomotic leakage ($p < 0.05$).
**Conclusion:** This study revealed no increased risk for morbidity in patients with diabetes using conventional continuous insulin infusion therapy. However, more than 2 comorbidities including diabetes revealed increased risk for anastomotic leakage after esophagectomy. We will start closed loop system for perioperative blood glucose concentration.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**LIVER AND BILIARY III – POSTER EXHIBITION**

## P1101 DONOR TM6SF2 RS58542926 GENOTYPE IS AN INDEPENDENT RISK FACTOR FOR DEVELOPMENT OF STEATOSIS AFTER LIVER TRANSPLANTATION

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**Introduction:** Polymorphism rs58542926 c.449 C > T v TM6SF2 (transmembrane 6 superfamily member 2) is one of genetic factors predisposing to development of non-alcoholic fatty liver disease (NAFLD).
**Aims & Methods:** We aimed to evaluate the influence of both recipient and donor TM6SF2 rs58542926 genotypes on development of steatosis in liver transplant (LT) recipients. The study group included 272 adult LT recipients transplanted between 1995 and 2010, in whom occurrence of steatosis was evaluated by liver biopsy during first 5 post-transplant years. We analyzed TM6SF2 rs58542926 and PNPLA3 (patatin-like phospholipase 3) rs738409 genotypes of recipients and donors, and clinical and laboratory data. Patients with steatosis (≥5%; grade 1–3) were compared to patients without steatosis (<5%, grade 0).
**Results:** Steatosis (grade 1–3) was found in 166 patients (61.0%), 106 patients (39.0%) did not develop any steatosis (grade 0). The distribution of donor TM6SF2 rs58542926 genotypes differed significantly (p = 0.036) between patients with steatosis (CC/CT/TT 80.1/19.3/0.6%) and without steatosis (CC/CT/TT 91.5/8.5/0.0%). The distribution of recipient TM6SF2 rs58542926 genotypes was similar (p = 0.91) in patients with steatosis (CC/CT/TT 77.7/19.9/2.4%) and without steatosis (CC/CT/TT 76.4/21.7/1.9%). On multivariate analysis, donor non-CC TM6SF2 genotype (OR 3.22; 95%CI 1.42–7.99), donor non-CC PNPLA3 genotype (OR 1.87; 95%CI 1.08–3.27) and BMI 1 year after LT (OR 1.14; 95%CI 1.06–1.24) were independent risk factors of development of post-transplant steatosis. The effect of donor PNPLA G allele and donor TM6SF2 T allele was synergic, with OR 7.61 (95%CI 2.04–49.45) for presence of both donor risk alleles and OR 1.84 (95%CI 1.11–3.06) for presence of only one risk allele (PNPLA3 G allele or TM6SF2 T allele).
**Conclusion:** Donor non-CC TM6SF2 rs58542926 genotype is an independent risk factor of steatosis in liver transplant recipients. The effect of donor TM6SF2 genotype is synergic to the effect of donor PNPLA3 genotype.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1102 LEAN NON-ALCOHOLIC FATTY LIVER DISEASE (LEAN-NAFLD): CHARACTERISTICS AND RISK FACTORS FROM A COMMUNITY COHORT FOLLOW-UP STUDY

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**Introduction:** Non-alcoholic fatty liver disease (NAFLD) is usually associated with obesity. However, some NAFLD patients are lean. We assessed the characteristics and risk factors for lean-NAFLD.
**Aims & Methods:** In a community cohort follow-up study (initial screening-2007, re-evaluation-2014), NAFLD was established on USS criteria and exclusion of alcohol overuse and secondary causes. Lean (BMI $<23\,kg/m^2$) and non-lean (BMI $\geq 23\,kg/m^2$) NAFLD were compared. The two groups were compared for differences in gender, diabetes, hypertension, hypertriglyceridemia, low-HDL, weight and waist circumference (WC) at baseline. They were also compared for differences in development of incident diabetes, hypertension, hypertriglyceridemia, low-HDL, and change in weight and WC.
**Results:** 678 (69.6%) individuals with NAFLD detected in 2007 presented for follow up in 2014. 78(11.5%) [males-32(41%); mean-age 53.7(SD-7.1) years] were lean and 600(88.5%) [males-191(31.8%); mean-age 52.3(SD-7.5) years] were non-lean. Hypertension (p = 0.007) and a smaller WC (<90 cm for males, <80 cm for females) (p < 0.001) were associated with lean-NAFLD. After 7 years, change in BMI was less (p = 0.022) among lean-NAFLD. There were no differences in change in WC or incident metabolic co-morbidities. Of those who did not have NAFLD in 2007, 746 developed incident NAFLD in 2014; lean-NAFLD 193/746 (25.9%) [males-100(51.8%); mean age 59.6(SD-7.5) ], non-lean-NAFLD 553/746 (74.1%) [males-201(36.3%); mean age 58.2(SD-7.7) ]. On logistic regression analysis, presence of diabetes (p = 0.002, OR 2.1) and raised WC (p = 0.003, OR 1.7) were associated with incident lean-NAFLD.
**Conclusion:** Among individuals with NAFLD, lean-NAFLD is associated with hypertension and smaller WC. In the community, diabetes and bigger WC predict incident lean-NAFLD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1103 NON-ALCOHOLIC FATTY LIVER DISEASE WITH AND WITHOUT METABOLIC SYNDROME: DIFFERENT PHENOTYPES WITH DIFFERENT LONG-TERM OUTCOMES

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**Introduction:** Non-alcoholic fatty liver disease and metabolic syndrome are shown to increase the risk of cardiovascular diseases and type 2 diabetes (1). There is a great overlap between these two diseases (2).
**Aims & Methods:** The present study was aimed to examine the cardiometabolic prognosis of non-alcoholic fatty liver disease with and without metabolic syndrome. Middle-aged subjects (n = 958) were divided into four subgroups, those with non-alcoholic fatty liver disease and metabolic syndrome, those with either non-alcoholic fatty liver disease or metabolic syndrome, and to healthy controls. The follow-up time for cardiovascular events was about 16 years. After approximately 21 years the cardiac ultrasound and laboratory parameters were re-analyzed and new type 2 diabetes cases were recorded.
**Results:** Those with both diseases were at the greatest risk for cardiovascular events (p < 0.001). Compared to healthy controls, only those with metabolic syndrome, with or without non-alcoholic fatty liver disease, were at increased risk for the development of type 2 diabetes (p < 0.001) and for an increase in left ventricular mass index (p = 0.001 and p = 0.005, respectively). The cardiometabolic risk in subjects with non-alcoholic fatty liver disease only was quite similar to that in healthy controls.
**Conclusion:** Non-alcoholic fatty liver disease with metabolic syndrome implies considerable risk for cardiovascular diseases, type 2 diabetes and the increase of left ventricular mass index whereas non-alcoholic fatty liver disease without metabolic syndrome does not.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1104 A NOVEL MUTATION OF *APOB* GENE ASSOCIATED WITH NEUROLOGICAL MANIFESTATIONS IN FAMILIAL HYPOBETALIPOPROTEINEMIA

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**Introduction:** Familial hypobetalipoproteinemia (FHBL) is monogenic, co-dominant disorder, characterized by reduced serum levels of total cholesterol, low density lipoproteins and apolipoprotein B. Clinical phenotypes of FHBL are related to number of defective apoliporotein B (APOB) alleles, and in some patients, except of liver disease, a range of extrahepatic symptoms can appear.
**Aim:** Genetic analysis of the APOB gene and ophtalmological diagnostics in family members with FHBL and neurological disorders were performed.
**Method:** Five relatives with FHBL were examined: proband with long-lasting asymptomatic steatohepatitis who developed dysarthria and finally severe extrapyramidal syndrome with dysphagia and ataxia, his two children with liver steatosis/steatohepatitisa and mild head/hand tremor and two grandchildren. A sequencing analysis of the whole coding region of the APOB gene, including flanking intronic regions, was performed using the next generation sequencing (NGS) method. An ophthalmological examination contained electrophysiological tests: pattern and flash full-field electroretinography (PERG, FERG), and pattern visual evoked potentials (PVEP).
**Results:** NGS identified the presence of not yet reported, pathogenic according to the American College of Medical Genetics and Genomics (ACMG) recommendations, heterozygous splicing variant c.3696+1 G > T. Two known heterozygous missense variants c.2188G > A, p.(Val730Ile), and c.8353A > C, p.(Asn2785His) in the APOB gene were also detected. The same pathogenic splicing variant was identified in affected proband's relatives. In the PERG examination, in all patients, a delay in implicit time, abnormally low amplitudes of a and b waves in both the scotopic and the photopic conditions were found and and reduced amplitudes of P50 and N95 were noted. In the proband and his children prolonged P100 latency was occurred in PVEP examination.

**Conclusion:** The newly identified splicing variant c.3696+1 G>T can be associated with observed autosomal, dominant FHBL with coexisting neurological symptoms. According to the literature and mutation databases, both identified missense variants could be excluded as the main cause of observed clinical signs. Electroretinography examination is a sensitive method for detection of early neuropathy, therefore should be recommended in care of patients with FHBL.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1105 LOW SERUM MAGNESIUM CONCENTRATION IS INDEPENDENTLY ASSOCIATED WITH NON ALCOHOLIC FATTY LIVER DISEASE AND NON ALCOHOLIC STEATOHEPATITIS

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**Introduction:** The pathogenesis of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) has not been well recognized. Low serum magnesium has been previously shown to be associated with oxidative stress and insulin resistance. Magnesium is also involved in metabolism of lipids.
**Aims & Methods:** This study aimed to investigate the association between serum magnesium concentration and hepatic steatosis in the forms of NAFLD and NASH. A cross-sectional study was conducted between September 2012 and September 2015 at Namazi hospital, Shiraz, Iran. Study subjects were healthy individuals who had undergone liver biopsy for evaluation of liver histology as a routine pre-transplant check up before living related liver transplantation. Liver function tests, age, gender, weight, height, fasting plasma glucose, magnesium, and lipid profile were recorded. Liver biopsy specimens were reviewed by an expert pathologist for hepatic steatosis and steatohepatitis. Individuals with a history of chronic liver disease, hepatitis B or C infection, hepato-billiary cancers, those with >20 grams/day alcohol consumption, and individuals receiving medications known to cause hepatic steatosis were excluded from the study.
**Results:** Totally 226 individuals (143 female and 83 male) were included. Eighty two individuals (36.2%) had hepatic steatosis and 22 (9.7%) individuals had steatohepatitis in liver histology. Mean age of individuals with and without hepatic steatosis were $33.28 \pm 7.55$ and $31.72 \pm 6.56$ years respectively ($P = 0.11$). In univariate analysis higher weight ($70.80 \pm 10.79$ versus (vs.) $63.44 \pm 9.57$ kilograms, $P = 0.0001$), increased cholesterol ($179.50 \pm 35.35$ vs. $166.04 \pm 36.50$ mg/dL, $P = 0.009$), triglyceride ($132.90 \pm 79.68$ vs. $93.10 \pm 46.78$ mg/dL, $P = 0.0001$), fasting plasma glucose (FPG) ($92.12 \pm 11.21$ vs. $87.02 \pm 10.21$ mg/dL, $P = 0.001$), alanine aminotransferase (ALT) ($22.59 \pm 12.01$ vs. $17.69 \pm 11.16$ IU/L, $P = 0.002$), alkaline phosphatase ($213.19 \pm 73.31$ vs. $183.22 \pm 62.65$ IU/L, $P = 0.001$) and lower serum magnesium ($2.01 \pm 0.35$ vs. $2.23 \pm 0.31$ mg/dL, $P = 0.0001$) were associated with hepatic steatosis ($P > 0.05$). In multivariate logistic regression analysis, higher FPG, higher alkaline phosphatase and lower serum magnesium concentration were independently associated with hepatic steatosis (Table). In regression analysis, lower serum magnesium concentration was also independently associated with steatohepatitis compared to those without steatohepatitis ($1.80 \pm 0.48$ mg/dL and $2.18 \pm 0.31$ mg/dL) (OR: 0.11; 95% CI: 0.02–0.41, P-Value = 0.001).

| | Odds ratio (OR) | **95% Confidence interval** (CI) | **P-Value** |
|---|---|---|---|
| Weight | 1.03 | 0.99–1.07 | 0.122 |
| Triglyceride | 1.006 | 0.99–1.01 | 0.089 |
| Cholesterol | 0.99 | 0.98–1.01 | 0.768 |
| Alanine aminotransferase | 1.009 | 0.97–1.04 | 0.608 |
| Alkaline phosphatase | 1.01 | 1.003–1.018 | 0.004 |
| Fasting plasma glucose | 1.05 | 1.01–1.10 | 0.012 |
| Magnesium | 0.05 | 0.01–0.32 | 0.001 |

**Conclusion:** Lower serum magnesium concentration was associated with non-alcoholic fatty liver disease and non-alcoholic steatohepatitis and can be targeted for future treatments.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1106 GENES AND ENVIRONMENTAL FACTORS INVOLVEMENT IN DEVELOPMENT OF NAFLD

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**Introduction:** Non-alcoholic fatty liver disease is considered a major public health and the natural course of the disease is possible influenced by the interaction of genetic and environmental factors. Aim of our study was to identify the involvement of genetic factor in the development of NAFLD.
**Aims & Methods:** We included 138 subjects with NAFLD and 125 age and sex-matched healthy controls. In both groups we evaluated anthropometric measures, aminotransferases level, presence of diabetes mellitus or metabolic syndrome, insulin resistance and the PNPLA3 gene polymorphism. Metabolic syndrome was defined according to IDF criteria and for insulin resistance we used HOMA-IR index. The genotyping assays were performed using predesigned TaqMan SNP Genotyping Assays.
**Results:** All 138 patients with hepatic steatosis (39 men and 99 women, mean age 49 +/- 13 years) 107 (77.53%) were obese, 120 patients (86.95%) had metabolic syndrome, 53 (38.4%) were diabetics and 81% (58.69%) had elevated liver enzymes.The genotype frequencies for PNPLA3 rs738409 polymorphism in the study group was [CC] (59.42%)> [CG] (32.41%)> [GG] (7.97%).The [CG] genotype carriers had a 1.7 times higher risk of developing hepatic steatosis, compared with the [CC] genotype OR 1.768 (95% CI; 1.006–3.110) ($p = 0.046$). The PNPLA3 polymorphism was associated with an increased risk of hepatic steatosis in patients with BMI $< 30\,kg/m^2$, compared with the control population, when the risk allele [G] carriers were compared with the [C] allele carriers ($p = 0.038$). By comparing the subgroup with steatosis without obesity with the subgroup with steatosis and BMI $\geq 30\,kg/m^2$, we have noticed that the [G] allele carriers compared to the [CC] homozigotes in the dominant model, have a 2.5 times higher risk of developing hepatic steatosis ($p = 0.025$) OR); 2.514 (1.112–5.685). [G] risk allele was significantly associated with the risk of hepatic steatosis in patients without metabolic syndrome ($p = 0.005$) and without insulino-resistance ($p = 0.033$). Also, we found no difference in cholesterol, triglycerides, aminotransferases and gamma-GT levels in [G] allele carrier vs [CC]
**Conclusion:** The [G] allele carriers have a 3 times higher risk of developing hepatic steatosis in the absence of obesity, insulin resistance, or metabolic syndrome. Patients with similar metabolic risk factors (diet, obesity, insulin resistance) differ largely in terms of disease phenotype and progression of disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1107 ELEVATED AMINOTRANSFERASE LEVEL IS ASSOCIATED WITH LOW BONE MINERAL DENSITY IN KOREA USING DATA FROM NATIONWIDE SURVEY

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**Introduction:** Elevated liver aminotransferase level was useful indicators for liver disease burden. The aim of the present study was to investigate whether serum aminotransferse level was associated with bone mineral density (BMD) among general adults in Korea.
**Aims & Methods:** The study subjects were 17481 adult who participated in the Korea National Health and Nutrition Examination Survey (2008–2011). Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentration were defined as >30 IU/L for men and >19 IU/L for women. Low BMD was defined as a T-score of –1.0 or less. Descriptive analysis and multiple logistic regression analysis were used to investigate the association between aminotransferease level and BMD.
**Results:** The proportions of elevated ALT and AST were 25.6% and 31.0%, respectively. Mean BMD at total hip, lumbar spine and femoral neck were $0.03 \pm 1.06$, $-0.73 \pm 1.31$ and $-0.70 \pm 1.19\,g/cm^2$, respectively. The proportions of low BMD at total hip, lumbar spine and femur neck were 15.8%, 40.4% and 40.2%, respectively. After adjusting for covariates, elevated ALT was significantly associated with low BMD at lumbar spine (aOR = 1.22, 95% CI = 1.12–1.33) and femur neck (aOR = 1.21, 955 CI = 1.10–1.33), respectively. And elevated AST was significantly associated with low BMD at total hip (aOR = 2.70, 95% CI = 2.25–3.23), lumbar spine (aOR = 1.40, 95% CI = 1.28–1.52), and femur neck (aOR = 1.25, 95% CI = 1.15–1.37), respectively.
**Conclusion:** Elevated serum aminotransferase level was independently associated with low bone mineral density among general adults in Korea.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1108 CONTRIBUTION OF B-LYMPHOCYTE ACTIVATING FACTOR TO INSULIN RESISTANCE IN PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS

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**Introduction:** Approximately 20–40% of patients with nonalcoholic steatohepatitis (NASH) have antinuclear antibodies (ANAs) in their sera. However, the relationship between ANA status and insulin resistance remains uncertain in those patients.
**Aims & Methods:** Twenty-five patients with NASH were enrolled in this study. Degrees of hepatic fibrosis and steatosis were evaluated by the classification proposed by Brunt and colleagues. Obesity and insulin resistance were estimated by calculating body mass index (BMI) and the value of HOMA-IR, respectively. Simplified scoring system was used for the diagnosis of autoimmune hepatitis (AIH).
**Results:** Ten of 25 (40%) patients with NASH had ANAs. However, only one patient was diagnosed as AIH among the patients with NASH seropositive for ANAs. Serum IgG ($1833 \pm 471$ vs $1292 \pm 269$ mg/dl, $p = 0.0055$) and B-

lymphocyte activating factor (BAFF) levels were significantly higher in NASH patients with ANAs than in NASH patients without ANAs. NASH patients seropositive for ANAs had significantly higher value of HOMA-IR than NASH patients seronegative for ANAs ($6.81 \pm 3.46$ vs $4.01 \pm 2.57$, $p = 0.0305$). Interestingly, a close correlation between serum BAFF level and the value of HOMA-IR was observed in those patients ($r = 0.729$, $p = 0.0168$). However, no significant differences in obesity, serum ALT level, and the degrees of hepatic fibrosis and steatosis were found between the groups of NASH patients seropositive and seronegative for ANAs.
**Conclusion:** These data suggest that NASH patients with ANAs may have more severe insulin resistance by way of elevation of serum BAFF levels.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1109 HIP FRACTURE RISK IN PEOPLE WITH ALCOHOLIC CIRRHOSIS COMPARED WITH THE GENERAL POPULATION: A POPULATION-BASED COHORT STUDY

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**Introduction:** While numerous studies have shown an association between chronic liver disease and osteoporosis few have documented accurately the risks of osteoporotic fracture in patients with alcoholic liver disease and none have compared incidence rates to the general population. We performed a cohort study using linked primary and secondary care data collected in England to quantify the excess fracture risk in people with alcohol-related cirrhosis.
**Aims & Methods:** We selected 3,416 patients with a diagnostic code for alcohol related cirrhosis within the linked Clinical Practice Research Datalink and Hospital Episodes Statistics database (April 1997 and June 2014) and 34,160 age-, sex- and practice-matched controls. We estimated absolute hip fracture rates and examined hazard ratios for patients with cirrhosis versus general population controls using Cox proportional hazards, adjusted for age, sex and drug use. Analyses were stratified by severity of disease.
**Results:** There was a 5-fold increased risk of hip fracture for the cirrhosis cohort compared with the general population (absolute rate 11.0 per 1000 person years; adjusted HR = 5.4 (95%CI[4.3, 6.8]). The absolute excess rates of fracture were 8.5 hip fractures per 1000 person years. Fracture risk was associated with disease severity such that the hazard ratio of hip fractures was almost twice as high in patients with decompensated cirrhosis than in those with compensated cirrhosis (HR decompensated cirrhosis 7.8 (95% CI [5.9, 10.3]); compensated cirrhosis3.8 (95% CI [2.8, 5.3]).

| | Absolute fracture rates (95% CI) per 1000 person years | Adjusted hazard ratio for hip fracture (95% CI) |
|---|---|---|
| Alcoholic cirrhosis cohort | 11.0 [9.0, 13.5] | 5.4[4.3, 6.8] |
| Compensated | 8.2 [6.0, 11.2] | 3.8 [2.8, 5.3] |
| Decompensated | 14.5 [11.2, 18.8] | 7.8 [5.9, 10.3] |
| Control population | 2.5 [2.2, 2.7] | 1.0 |

**Conclusion:** People with alcohol-related cirrhosis are at increased risk of hip fracture compared with the general population and those with more severe disease have an even greater risk. These findings imply that consideration should be given to interventions in this group to reduce fracture risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1110 HEPATIC ENCEPHALOPATHY IS ASSOCIATED WITH PERSISTENT LEARNING IMPAIRMENTS DESPITE ADEQUATE MEDICAL TREATMENT: A MULTI-CENTER, INTERNATIONAL STUDY

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**Introduction:** Hepatic encephalopathy (HE) is considered reversible regarding mental status but may not be cognitively in single-center studies
**Aims & Methods:** Aim: To evaluate persistence of learning impairment in prior HE compared to those who never experienced HE (no-HE) in a multi-center study. **Methods**: 174 outpatient cirrhotics from 3 centers (94 Virginia, 30 Ohio, 50 Rome, 36 prior HE) underwent Psychometric hepatic encephalopathy score (PHES) and Inhibitory control (ICT) testing at baseline and then at least 7 days apart. ICT learning (change in 2nd half lures compared to 1st half) was compared between patient groups at both visits. Change in the PHES individual sub-tests and total score between visits were compared in both groups. US vs. Italian trends were also analyzed.
**Results:** HE patients had worse PHES and ICT results compared to no-HE patients at baseline. Significant improvement (1st 7.1 vs. 6.2, 2nd half, $p < 0.0001$) was observed in no-HE, but not in HE (1st 7.9 vs. 7.8, $p = 0.1$) at baseline. At retesting (median 20 days later), no-HE patients continued with significant learning (1st6.0 vs. 2nd half 5.4, $p < 0.0001$), while HE patients again did not improve (1st 7.8 vs. 2nd half 6.9, $p = 0.37$). Between visits, no-HE patients improved significantly on 4 PHES sub-tests and overall score, while HE patients only improved on 2 sub-tests with similar overall PHES score. Trends were similar between US and Italian subjects.
**Conclusion:** In this multi-center study, prior HE patients showed persistent significant learning impairment compared to those without prior HE, despite adequate medical therapy. This persistent change should increase efforts to reduce the first HE episode.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1111 THE EFFECT OF SYNBIOTIC AND PROKINETIC ON INTESTINAL PERMEABILITY, ENDOTOXEMIA AND CHILD-PUGH SCORE IN PATIENTS WITH LIVER CIRRHOSIS: A PROSPECTIVE COHORT STUDY

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**Introduction:** Increased intestinal permeability and small intestinal bacterial overgrowth are important pathophysiological factors of bacterial translocation in liver cirrhosis. Several clinical trials have shown an association among increased intestinal permeability, severity of liver cirrhosis and increased endotoxemia levels. Therapeutic modulations of intestinal microbiota with probiotics have demonstrated efficacy in reduction of endotoxemia in cirrhotics and decrease of bacterial infections after liver transplantation. Prokinetics were proved to accelerate gastrointestinal motility and reduce small intestinal bacterial overgrowth in patients with liver cirrhosis.
**Aims & Methods:** The aim of the study was to investigate the effect of synbiotic and prokinetic on intestinal permeability, endotoxemia levels and the severity of liver cirrhosis in patients with liver cirrhosis. 78 patients with liver cirrhosis were randomized to receive synbiotic composition of two fibers and probiotic bacteria *Lactobacillus plantarum*, *L. Rhamnosus*, *L. Bulgaricus*, *L. Acidofilus*, *Bifidobacterium* (n = 31), synbiotic and prokinetic domperidon (n = 27) or none of them (n = 20) for 30 days. The patients underwent standard clinical examination, had blood tests performed and the level of endotoxin was determined. Their intestinal permeability was measured by lactulose/manitol excretion ratio (LMR) from the urine samples that were collected before and after the treatment. During the follow-up period the occurrences of bacterial infections were recorded. 32 healthy controls (HC) were included in the study to assess intestinal permeability and a level of serum endotoxin.
**Results:** 48 (61.5%) patients had Child A, 19 (24.4%) Child B and 11 (14.1%) Child C with the mean age of 54 (SD = 11.6) years in the study. The Child-Pugh functional class overall improved in 29% of patients, and this improvement reached statistical significance in two patients groups treated both with synbiotic alone and in combination with domperidon. Intestinal permeability was increased in 7 (10.1%) patients. LMR was higher in patients than in healthy controls (patients vs HC = 0.0123 [0.0023–0.0508; 0.0103] vs 0.0069 [0.0003–0.0242;0.0103]; $p = 0.027$). However, the LMR of the patients did not significantly varied among different Child classes neither among different liver cirrhosis etiologies nor among patients groups. The endotoxin levels were comparable in three patients groups and did not significantly differ before and after the treatment (endotoxin before vs after the treatment = 0.5524 [SD = 0.299] vs 0.5555 [SD = 0.299], $p = 0.914$). During the follow-up period the occurrences of infections did not vary significantly in the patients groups nor in the patients with normal and increased intestinal permeability.
**Conclusion:** We proved that short-term treatment with synbiotics alone or in combination with domperidon was significantly effective and improved liver cirrhosis severity in 29% of cases. However, the treatment did not affect intestinal permeability neither endotoxemia levels nor occurrences of infections.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1112 CLIF-C AD SCORE WAS NOT CONSISTENTLY BETTER THAN THE TRADITIONAL MODELS IN PREDICTING 30 AND 90 DAY MORTALITY IN CIRRHOTIC PATIENTS WITH ACUTE DECOMPENSATION WITHOUT ACLF

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**Introduction:** Recently the EASL-CLIF Consortium has developed and validated the CLIF-C acute decompensation (AD) score, with the aim of predicting mortality in cirrhotic patients with acute decompensation (AD) without evidence of acute-on chronic liver failure (ACLF) .[1]

**Aims & Methods:** To compare the accuracy of CLIF-C ADs with some of the previously validated models: Child-Pugh, MELD, iMELD, Refit-MELD, MELD-Na, MESO and Refit-MELD-Na; for predicting the 30 and 90-day mortality in hospitalized cirrhotic patients without ACLF. Retrospective cohort study that evaluated all admissions due to decompensated cirrhosis in 2 centers between 2011 and 2014. The presence of ACLF was defined according to the CLIF Consortium Organ Failure Score. Demographic, analytical and medical records were reviewed. At admission (<24 h) each score was assessed, and the discrimination ability was compared by using Areas Under the Roc Curves (AUROCs) for the 30 and 90-day mortality.

**Results:** We identified 565 cirrhotic patients with acute decompensation without ACLF; the most common etiology was alcohol (64.2%), followed by hepatitis C (21.3%); 37.7% met criteria for infection at admission; 27.3% presented gastrointestinal bleeding (esophageal variceal bleeding=86%); 30 and 90-day mortality were respectively, 10.3% and 31.1%. When evaluated the 30-day mortality CLIF-C ADs (AUC = 0.689; 95% CI = 0.647–0.728) presented the highest discrimination ability, although when compared AUROCs with the other scores, for the exception of MELD (AUC = 0.605; p = 0.0296), it was not significantly better. When analyzed the 90-day mortality, CLIF-C ADs (AUC = 0.672; 95% CI = 0.630–0.712) was not significantly different from the other tested models.

**Conclusion:** Although the new CLIF-C ADs reveled a good discrimination ability in predicting 30 and 90 day-mortality in hospitalized cirrhotic patients without ACLF, it was not significantly better than the other tested prognostic models with the exception of MELD in predicting 30-day mortality.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1113 THE ROLE OF THE MEAN PLATELET VOLUME AS A PREDICTION MARKER FOR SPONTANEOUS BACTERIAL PERITONTIS

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**Introduction:** Ascitic fluid cell analysis is considered to be the gold standard method for diagnosing spontaneous bacterial peritonitis (SBP). Recent studies have reported mean platelet volume (MPV) as a marker for systemic inflammation that does not suffer the influence of the different stages of cirrhosis, with a good accuracy for predicting SBP. Nonetheless, most studies excluded factors that could influence its value, and that literature reports as having an high prevalence in patients with cirrhosis (previously antibiotic therapy, comorbidities as heart failure, diabetes, hyperlipidemia and neoplasia), and so, the real value of MPV as a screening test for SBP still needs to be tested. [1–3]

**Aims & Methods:** To assess the value of MPV as (1) an inflammation marker in decompensated chronic liver disease secondary to bacterial infection (2) its ability to predict SBP. Retrospective multicentric study that analyzed all admissions secondarily to decompensated chronic liver disease, between 2011 and 2014. By using areas under the ROC curves, we compared the variables white blood count (WBC), c-reactive protein (CRP) and MPV for predicting SBP, and compared them. We defined infections according to standard criteria.

**P1112**

| | CLIF-C ADs(95% CI) | Child-Pugh(95% CI) | MELD(95% CI) | MELD-Na(95% CI) | iMELD(95% CI) | MESO(95% CI) | REFIT MELD(95% CI) | REFIT MELD-Na(95% CI) |
|---|---|---|---|---|---|---|---|---|
| 30-day mortality | 0.689 (0.647–0.728) | 0.665 (0.622–0.705) | 0.605 (0.561–0.647) | 0.658 (0.616–0.699) | 0.666 (0.624–0.706) | 0.626 (0.583–0.668) | 0.637 (0.594–0.678) | 0.673 (0.631–0.713) |
| p value vs. CLIF-C ADs | | 0.5905 | 0.0296 | 0.3442 | 0.4391 | 0.0830 | 0.1519 | 0.6135 |
| 90-day mortality | 0.672 (0.630–0.712) | 0.649 (0.606–0.690) | 0.644 (0.601–0.685) | 0.689 (0.647–0.729) | 0.707 (0.666–0.746) | 0.662 (0.619–0.702) | 0.670 (0.627–0.710) | 0.700 (0.659–0.739) |
| p value vs. CLIF-C ADs | | 0.4422 | 0.2966 | 0.4238 | 0.0500 | 0.6830 | 0.9233 | 0.1565 |

**Results:** We identified 605 patients, 326 with active infection and 118 with SBP. WBC (10.638 vs 7.560 x109/L; p = 0.000) and CRP (42.48 vs 17.66 mg/L p = 0.000) were statistically higher in the group of patients with active infection compared to uninfected. Although MPV was higher in the infected group of patients, it was not a statistically significant difference (10.08 vs 9.77 fL; p = 0.072). When matched patients with SBP versus uninfected and patients with other infections, WBC (10.792 vs 8.837 x109/L; p = 0.001), CRP (55.94 vs 25.10 mg/L; p = 0.000) and MPV (10.71 vs 9.74 fL; p = 0.000), were statistically higher. Within the group of patients with active infection, those with SBP, presented statistically higher values of MPV (10.71 vs 9.70 fL; p = 0.000) compared to the other infections. Although MPV was not correlated to 30-day mortality, it was correlated to 90-day mortality (Rs = 0.137; p = 0.001). In order to predict SBP, the areas under the ROC curves were: WBC = 0.574; CRP = 0.729 and MPV = 0.684. When compared the discriminating ability, no statistically significant difference was found between CRP and MPV (p = 0.071), but they were both superior to WBC (respectively, p = 0.000 and p = 0.033).
**Conclusion:** 1) MPV seems to be a good marker for the presence of systemic inflammation; 2) although patients with SBP presented higher values of MPV, our data does not support the general use of MPV as a screening method for SBP. Nevertheless, MPV presented an average discriminating power for SBP prediction, similar to CRP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1114 ASSESSMENT OF PROGNOSTIC SCORES IN ALCOHOLIC HEPATITIS


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**Introduction:** Excessive alcohol consumption is associated with a vast spectrum of hepatic manifestations, including alcoholic fatty liver disease, alcoholic hepatitis (AH), and cirrhosis. AH in its severe form, presents a high morbidity and mortality and there are several prognostic models validated for predicting prognosis and for guiding treatment decisions.
**Aims & Methods:** To compare in patients with AH, the accuracy of Chronic Liver Failure Consortium organ failure (CLIF-C OF) score with the traditional models: Model for End-Stage Liver Disease (MELD), Maddrey Discriminant Function (MDF) and Age-Bilirubin-INR-Creatinine (ABIC) index, for predicting in the first 24 h of hospitalization, the 30 and 90 day-mortality. We performed a retrospective analysis of 58 patients with the diagnosis of AH admitted in our department between 2010 and 2015. AH was defined according to clinical and analytical criteria: Bilirubin > 1.5 mg /dL; ratio AST / ALT > 1.5 with AST > 75UI/L; history of chronic alcohol abuse; absence of other causes of chronic liver disease, including viral infection. We excluded hospitalizations for bleeding and patients with known neoplasia. Receiver operating characteristic (ROC) curves were generated to assess the prognostic utility of each model.
**Results:** At admission, the mean CLIF-C OFs, MELD, MDF and ABIC were respectively, 8 ± 2, 20 ± 6, 45 ± 30 and 8 ± 1. The Thirty-day and 90-day mortality was 25.9% and 43.1%, correspondingly. In the prediction of 30-day mortality, CLIF-C OFs presented an area under the curve (AUC) of 0.796 (95% CI: 0.670 to 0.891). Although it was significant better than ABIC (AUC = 0.625; p = 0.0433), its discrimination ability was not superior to MELD (AUC = 0.695; p = 0.0814) and MDF (AUC = 0.676; p = 0.1158). In assessing the 90-day mortality, the CLIF-C OFs also presented the highest discrimination ability (AUC = 0.73; 95% CI: 0.604–0.843). When compared, it was significant better than MDF (AUC = 0.633;p = 0.0077) and similar to MELD (AUC = 0.656; p = 0.2078) and ABIC (AUC = 0.645; p = 0.2436).
**Conclusion:** In our sample the CLIF-C OFs was the best model to predict 30 and 90-day mortality. If our results are validated in other cohorts, we should eventually aim to delevop prospective studies that could designate cut-off points like in MDF, for guiding treatment decisions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1115 PORTAL VEIN THROMBOSIS AND CIRRHOSIS PROGRESSION: WHAT IS THE RELATION?


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**Introduction:** The incidence of portal vein thrombosis (PVT) in cirrhotic patients reported in the literature varies (0.6 to 30%). The role of PVT in cirrhosis progression is controversial and recently it has been suggested that PVT does not depend on previous progression of liver disease nor is responsible for its future progression.[1]
**Aims & Methods:** We aimed to evaluate the relation between PVT and progression of liver disease. Retrospective observational study including Child Turcutte Pugh (CTP) A and B cirrhotic patients followed in outpatient clinic between March 2008 and August 2015. Progression of cirrhosis was defined as: "de novo" ascites or hepatic encephalopathy, variceal bleeding, bilirubin > 2.6 mg/dL, prothrombin rate < 45%, serum albumin < 2.8 mg/dL and/or creatinine > 1.3 mg/dL.
**Results:** 107 patients were included (male sex 54.2%, mean age 55.5 ± 14.4), with a median follow-up of 62.5 months (IQR 39.0–82.3). Alcohol was the etiology of cirrhosis in 52.3%, 76.6% were CTP A. 8.4% had PVT and 44.4% of those patients were anticoagulated. The overall mortality was 20.0% and was not significantly superior in PVT patients (p = 0.776). PVT was associated with liver disease progression (p = 0.034) and this association remained significant in multivariate analysis (OR 4.423 95%IC 1.014–18.424), however only 44.4% of the patients with PVT had cirrhosis progression during or after the event. PVT was not associated with liver disease progression before the thrombotic event (p = 0.559). The progression of the disease was associated with age (p = 0.037), hepatic encephalopathy at the inclusion (p = 0.05), but not the development of previous or concomitant PVT (p = 0.194).
**Conclusion:** PVT and cirrhosis progression might be two common events of the disease course but do not seem to have a cause-effect relation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1116 DIAGNOSTIC ACCURACY OF NON-INVASIVE TESTS FOR PREDICTING ESOPHAGEAL VARICES IN PATIENTS WITH HCV-RELATED CIRRHOSIS


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**Introduction:** Esophageal varices (EV) screening is recommended in cirrhotic patients. In a non-invasive era of hephatology clinical practice, we aimed to assess the performance of non-invasive test in predicting EV on cirrhotic patients with Chronic hepatitis C.
**Aims & Methods:** Retrospective study evaluated cirrhotics for their liver stiffness (FibroScan®), platelet count (PC), Fib-4, APRI and AST/ALT ratio. Upper endoscopy was preformed for detection of EV. Performance was measured by: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under the ROC curve (AUROC) and accuracy.
**Results:** The study included 144 HCV-related cirrhotic patients, 73% male with mean age of 59[28–88] years. FibroScan was performed for staging of chronic hepatitis C. All tests were preformed within 3 months of upper endoscopy. AST/ALT ratio did nor correlate with presence of EV. FS, CP, Fib-4 and APRI showed statistical significance in predicting EV ($p < 0.05$).Platelets count and Fib-4 obtained higher NPV, 91.3% and 89.7% respectively. The combination of FS > 20 and PC < 150x10 ^ 3 / uL obtained VPN of 87% and increased the accuracy to 78.3% for predicting EV. The presence of FS > 20 and PC < 150 x10 ^ 3 / uL is associated with an increased risk of EV OR: 11.36 (95% CI: 4.56 to 28.02).
**Conclusion:** FibroScan, Platelet Count and FIB-4 had a satisfactory performance in predicting LV. The combination of FibroScan and Platelet Count increased accuracy for predicting EV. PC was the best predictor for absence of EV. Their use in clinical practice may allow a better selection of patients for endoscopic screening portal hypertension. These results are consistent with the recent tendency to use non-invasive methods in hepatology clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1114**

| | CLIF-C OFs (95% CI) | **MELD (95% CI)** | MDF (95% CI) | **ABIC (95% CI)** |
|---|---|---|---|---|
| 30-day mortality p value vs. CLIF-C OFs | 0.796 (0.670–0.891) | 0.695 (0.561–0.809) 0.0814 | 0.676 (0.540–0.793) 0.1158 | 0.625 (0.488–0.749) 0.0433 |
| 90-day mortality p value vs. CLIF-C OFs | 0.736 (0.604–0.843) | 0.656 (0.520–0.776) 0.2078 | 0.633 (0.512–0.756) 0.0077 | 0.645 (0.509–0.767) 0.2436 |

**P1116**

| | Cut-offs | Sensibility | Specificity | PPV | NPV | Accuracy | AUROC |
|---|---|---|---|---|---|---|---|
| **FS(N = 120)** | ≥20(Kpa) | 75.6% | 65% | 49.1% | 85.7% | 68.3% | 0.717 (IC95% 0.614–0.820) |
| **PC(N = 144)** | <150x10^3/μL | 91.4% | 43.2% | 43.8% | 91.3% | 59% | 0.786 (IC95% 0.708–0.865) |
| **FIB-4(N = 144)** | ≥2 | 91.4% | 36.1% | 40.1% | 89.7% | 67.3% | 0.771 (IC95% 0.691–0.851) |
| **APRI(N = 144)** | ≥1.3 | 72.3% | 51.5% | 41.9% | 79.3% | 58.3% | 0.690 (IC95% 0.602–0.778) |

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### P1117 SPONTANEOUS BACTERIAL PERITONITIS IN CIRRHOTIC PATIENTS UNDER SECONDARY ANTIBIOTIC PROPHYLAXIS

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**Introduction:** Spontaneous bacterial peritonitis (SBP) was historically caused by Gram-negative bacteria (GNB) by enteral translocation. However, we are assisting to the emergency of SBP to Gram-positive bacteria (GPB) and Gram-negative resistant to quinolones, which could be related with prolonged antibiotic prophylaxis. Secondary antibiotic prophylaxis is recommended in high risk patients such as the ones with prior SBP episode.
**Aims & Methods: Aim –** Characterization of SBP in cirrhotic patients under secondary antibiotic prophylaxis and identification of predictor factors of SBP to multidrug resistant microorganisms **Methods** – Unicentric retrospective study of a cohort of patients admitted in a Gastroenterology ward with SBP under secondary antibiotic prophylaxis by a previous SBP episode between January/2009 and January/2015. Statistic analysis with SPSS v.23.
**Results:** 37 episodes of SBP were included corresponding to 24 patients. 83.3% were men with mean age of 64,5 years old (49–86). 78.4% had a recent previous hospitalar admission (≤ 30 days before). The average length of stay was 9,92 days. 83.8% had alcoholic cirrhosis etiology. 67.7% were Child-Pug C. 97.3% were receiving norfloxacin as antibiotic prophylaxis and 2.7% sulfamethoxazole/trimethoprim. Ascitic fluid culture was positive in 27% of patients: 80% by GNB being E. coli the most frequent isolated agent. 70% of the isolated bacteria were quinolone-resistant and 60% were third generation cephalosporin-resistant. 86.5% started antibiotic treatment with ceftriaxone but in 21.6% it was necessary an antibiotic adjustment. Quinolones resistant agents happened in patients with a more prolonged time of antibiotic prophylaxis (mean time of 9.7 months versus 2.4 months in non-resistant) and all of them had a previous recent hospitalar admissions. Mortality in SBP episode was 16.2% and 1 year-mortality was 77.4%.
**Conclusion:** SBP in patients under secondary antibiotic prophylaxis was associated with GNB quinolones-resistant. This microbiologic resistance seems to be associated with a more prolonged time of antibiotic prophylaxis. Mortality and 1 year-mortality were high.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1118 STUDY OF PRURITUS IN CHRONIC LIVER DISEASES

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**Introduction:** Pruritus is a common symptom in patients with liver diseases, however, there is a paucity of information regarding its frequencies among patients with various liver diseases and with various etiologies.
**Aims & Methods:** The aim of this study is to clarify the frequency and severity of pruritus, and effect of therapies including nalfurafine hydrochloride in various chronic liver diseases. A total of 288 patients with chronic liver diseases (157 males, 131 females, 64.8 ± 11.9 years' old) were included in the study. The study was performed using a questionnaire with itch scale sheet for asking the degree, time of itch, and the effect of therapies. Diagnoses of the subjects were as follows: chronic hepatitis (CH), 176; liver cirrhosis (LC), 21; hepatocellular carcinoma (HCC), 74; primary biliary cirrhosis, 6; others, 11. Etiologies of diseases were as follows: hepatitis B virus (HBV), 34; hepatitis C virus (HCV), 210; non-B, non-C, 44.
**Results:** The frequencies and severities of pruritus were as follows: none, 180 (62.5%); mild, 89 (30.9%); moderate, 15 (5.2%); severe, 4 (1.4%). Frequencies of pruritus were 31.8% in patients with CH, 46.3% with LC, and 50.0% with PBC. The rate was significantly higher in patients with LC than that with CH ($p < 0.05$). Frequencies did not differ between HBV and HCV in the present subjects (36.7% and 31.6%). Itch was felt mainly in nighttime in 65.7%, daytime in 9.8%, and both in 24.5%. Among patients with pruritus, 38.0% were treated by crèmes or lotions and 12.0% were with oral medicaments (antihistamine). Effect of therapies was limited in 56.3% of them. Four patients with moderate or severe pruritus were treated by nalfurafine hydrochloride, and the severity of pruritus was improved in all of them ($3.25 \pm 0.25$ to $1.50 \pm 0.29$, $p < 0.01$) by 6 grade-itch face score). Among 19 patients with moderate or severe pruritus, only 5 of them told the doctors the complaint of itch, and the doctors knew the patients' symptom of pruritus for the first time by the itch scale sheet of the present study in the rest 14 patients.
**Conclusion:** Pruritus was found in 37.5% of patients with chronic liver diseases, and the rate was high in LC and PBC, however, no difference was found between HBV and HCV. Many patients did not tell the doctors the complaint of pruritus. Nalfurafine hydrochloride is one of a therapeutic option in patients with limited effect by other therapies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1119 EVALUATION OF SERUM ZINC LEVEL IN PATIENTS WITH LIVER CIRRHOSIS IN DUHOK GOVERNORATE

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**Introduction:** Cirrhosis is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrous scar leading to progressive loss of liver function. It is most commonly caused by alcoholism and hepatitis B or C. Low serum zinc level is common in patients with liver cirrhosis and appears to be due to anorexia and reduced intake of animal proteins, increase in cytokines or hormones involved in zinc metabolism, increases in renal loss and poor absorption of nutrients due to portal hypertension.
**Aims & Methods:** To determine the serum zinc level in patients with liver cirrhosis in Duhok Governorate. This case control study was conducted on a population of 70 randomly selected sample of patients with liver cirrhosis from 1st of January 2015 to 30th of December 2015, who came for follow up in the Center of Gastrointestinal and Hepatic Disease, Duhok governorate, Iraq and those who admitted in the medical ward at Azadi General Teaching Hospital and 70 of matched healthy individuals as control group. The patients were interviewed and examined, and their blood samples taken for zinc level and assessment of Child–Pugh score was done for them.
**Results:** The mean zinc level in cases group was 73.11μg/dl versus 81.24 in control group ($P = 0.006$). The number of participants, who were low for zinc level was 29 (41.4%) versus 14 (20%) in cases and control groups respectively ($P = 0.006$). As severity of liver cirrhosis increased, the zinc level decreased, it was 2 (14.3%) in class A, versus 19 (43.2%) in class B, versus 8 (66.7%) in class C of Child Pugh score, the P value was significant at 0.024.
**Conclusion:** Hypozincemia is very common in patients with liver cirrhosis in Duhok. A routine biochemical assessment of serum zinc level in patients with

liver cirrhosis is an important step in the management of such patients which will potentially lead to reduction of the progression of their disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1120 PREDICTING OUTCOME IN ACUTE-ON-CHRONIC LIVER FAILURE USING ERYTHROPOIETIN LEVELS


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**Introduction:** Acute-on-chronic liver failure (ACLF) represents a major challenge for clinicians due to the fact that no single universally accepted diagnostic criteria exist. The illness is characterized by a rapid progression to multiple organ failure and a very high short-term mortality of 50–90%. Liver transplantation is the only therapeutic option to improve survival, but a large proportion of patients succumb while waiting on the transplant list. As a result, other therapeutic options are being investigated such as the use of erythropoietin (EPO). EPO is a pleiotropic cytokine known chiefly for its role in the stimulation of erythropoiesis, however, it also has a number of other functions including: cytoprotective, anti-apoptotic, anti-inflammatory and antioxidant activity. In addition it raises the level of calcium in the vascular endothelium, and stimulates the actions of angiotensin II, leading to enhanced perfusion and tissue healing.
**Aims & Methods:** The aim of this study was to predict the 28-day mortality outcome of patients with ACLF based on levels of EPO at admission and at 48 hours. This prospective cohort study, performed from January 1st 2014 to July 1st 2015, included 104 patients diagnosed with ACLF according to the EASL-CLIF criteria, at the Emergency Centre of the Clinical Centre of Serbia, Department for Gastroenterology and Hepatology, Belgrade, Serbia. The patients were divided into two groups based on the type of insult: Group A = gastrointestinal bleeding, and Group B = insult other than gastrointestinal bleeding. The control group consisted of patients with chronic stable liver failure. All patients underwent a complete biochemical workup, including measurement of EPO values on admission, along with calculation of relevant scores for assessing liver function and outcome in ACLF (Child-Pugh, MELD, MELD-Na, SOFA, APACHE II, CLIF C, and AoCLIF). Values of EPO in correlation to the type of acute insult and final outcome (28 day mortality rate) were analyzed.
**Results:** Group A (n = 31) had a mean age of 60.32 ± 9.29 years, and in Group B (n = 73), the mean age was 59.9 ± 10.19 years. The control group (n = 20) mean age was 61.1 ± 8.3 years. The underlining etiology of disease was alcohol abuse in majority of the patients (Group A = 80.6%, Group B = 76.7%, Control group- = 75%). The collected parameters for the test groups are presented in Table 1. The control group had expectedly lower values for all parameters assessed particularly EPO at admission 14.27 ± 13.45mIU/mL and EPO at 48 h 13.78 ± 9.96mIU/mL. Lethal outcome was observed in 15 (48.4%) patients from Group A, and in 37 (50.7%) patients from Group B. In Group A, patients with a lethal outcome had statistically significant higher values of EPO at admission (319.26 ± 326.58mIU/ml) and at 48 hours (136.83 ± 99.06mIU/mL), $p < 0.005$. In Group B, the EPO values were lower ($p = 0.002$) in patients with a lethal outcome (29.88 ± 34.6mIU/mL and 37.77 ± 49.2mIU/mL, respectively). For a cut-off EPO value of 30.65mIU/mL the sensitivity and specificity to predict lethal outcome was 87.5% and 57.4%, respectively.

**Table 1:** Levels of EPO and prognostic scores in test groups (n = 104)

| | Group A (n = 31) | Group B (n = 73) | p values |
|---|---|---|---|
| EPO (mIU/mL) | 293.62 ± 282.76 | 41.59 ± 50.91 | < 0.001 |
| EPO 48 h (mIU/mL) | 161.94 ± 170.36 | 41.39 ± 44.60 | < 0.001 |
| Child-Pugh | 10.74 ± 2.02 | 11.16 ± 1.72 | 0.279 |
| MELD | 20.29 ± 5.83 | 22.37 ± 6.68 | 0.135 |
| MELD-Na | 22.19 ± 5.97 | 24.58 ± 6.58 | 0.086 |
| SOFA | 9.10 ± 2.59 | 9.62 ± 2.59 | 0.351 |
| APACHE II | 14.03 ± 4.02 | 14.47 ± 4.31 | 0.634 |
| CLIF C | 55.87 ± 6.26 | 55.74 ± 8.21 | 0.943 |
| AoCLIF gr I | 6 | 13 | |
| AoCLIF gr II | 15 | 30 | 0.692 |
| AoCLIF gr III | 10 | 30 | |

EPO: Erythropoeitin, MELD: Model of End Stage Liver Disease, MELD-Na: Model of End Stage Liver Disease with Sodium, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II, CLIF C: Chronic Liver Failure - Consorcium ACLF score, AoCLIF: Acute-on-Chronic Liver Failure grade.

**Conclusion:** Patients suffering from ACLF without bleeding as an insult had significantly lower values of EPO, and based on our results, we can recommend that these patients would benefit most from EPO therapy. Taking into account the positive effects of EPO treatment in stimulating hepatic regeneration and improving hepatic function, further studies are necessary to solidify our data.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1121 SUBCLINICAL HYPOTHYROIDISM MAY BE AN INDEPENDENT RISK FACTOR FOR LIVER DECOMPENSATION IN CIRRHOTIC PATIENTS


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**Introduction:** Patients with end-stage liver cirrhosis are at risk for major events of decompensation (ascites, bleeding or encephalopathy). We aimed to investigate whether cirrhotic patients with hypothyroidism may show higher rate and earlier events of decompensation than those with normal thyroid function.
**Aims & Methods:** We enrolled cirrhotic patients with (n = 20 with 30 episodes of decompensation) and without hypothyroidism (n = 23), with a median follow up time of 292.5 days. For each patients, decompensation was considered as hospital re-admission for ascites, bleeding or encephalopathy, and we collected data about etiology of cirrhosis, age, sex, MELD score, presence of hepatocarcinoma and blood levels of T3, T4 and TSH hormones. Hypothyroidism was considered as compensated when TSH and thyroid hormones were in their normal range, while subclinical hypothyroidism was defined by high TSH in the presence of normal T3 and T4 levels. A Kaplan-Meier curve was plotted and, at univariate analysis, log-rank test for survival was applied. For multivariate analysis, Cox regression model was applied.
**Results:** Patients with hypothyroidism (both compensated and subclinical) had higher overall TSH levels ($p = 0.04$), but comparable values of T3 and T4 hormones ($p = 0.9$ and 0.16 respectively) compared to cirrhotic without hypothyroidism. The risk of hepatic decompensation was higher when hypothyroidism occurred (HR = 1.725, p log-rank = 0.035), and hospital readmission for cirrhotic with hypothyroidism was earlier (median time = 77.5 days) than those without (median time = 300 days). Subjects with subclinical hypothyroidism had shorter survival time than for compensated hypothyroidism (median 55 vs 210 days respectively, despite not significant $p = 0.14$). Cox multivariate analysis showed that none of considered variables affected survival time, except the presence/absence of hypothyroidism.
**Conclusion:** Hypothyroidisms (both compensated and subclinical) are an independent risk factor for hepatic decompensation. This factor could influence the course of liver disease independently from other well-known variables.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1122 IN SEARCH OF THE BEST PROGNOSTIC MODEL IN DECOMPENSATED CIRRHOSIS: WHAT IS THE VALUE OF C-REACTIVE PROTEIN?

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**Introduction:** Inflammation is an essential factor in the pathogenesis of decompensated cirrhosis and of acute-on-chronic liver failure (ACLF). As such, C-reactive protein (CRP) may have a key role on the evaluation of prognosis of this group of patients.

**Aims & Methods:** Retrospective study with inclusion of all patients admitted in a gastroenterology and hepatology unit between January 2013 and December 2015 due to decompensated cirrhosis (including but not limited to patients with ACLF criteria). Patients with overt infection at admission or hepatocellular carcinoma were excluded. Demographic, clinical and analytical (including CRP) data, prognostic scores [Model for end-stage liver disease (MELD) and MELD-Na), in-patient mortality (IPM) and mortality within 3 months of admission (M3) were collected. Statistical analysis was performed with SPSS 20.0.

**Results:** One hundred and 30 patients (80% males) with a median of age of 60.1 years were included; 16.5% of these patients had ACLF criteria. IPM was 13.1% and M3 22.2%. On exploratory analysis there were statistically significant differences between the median value of CRP in patients with and without IPM (1.85 versus 0.99 mg/dL; $p = 0.026$) and with and without M3 (1.89 vs 0.90 mg/dL; $p = 0.006$). In the logistic regression model, CRP only remained as an independent predictor for M3, with an increase of 15.7% on the odds of M3 for each increase of 1 mg/dL of CRP. On analysis of the receiver operating characteristic (ROC) curves, the best predictive model for both IPM and M3 was Meld-Na, with a strong discrimination power of 0.81 [confidence interval (CI) 95% 0.67–0.95;$p < 0.001$] and 0.78 (CI 95% 0.67–0.89; $p < 0.001$), respectively. CRP had a moderate discrimination power of 0.69 (CI95% 0.54–0.83;$p = 0.02$) and 0.68 (CI95% 0.57–0.80; $p = 0.004$) for IPM and M3, respectively. In a model incorporating Meld-Na and CRP, the discrimination power for IPM didn't improve in comparison to Meld-Na alone (0.79, CI95% 0.68–0.90; $p < 0.001$); there was a slight improvement in the discrimination power for M3 (0.79; CI95% 0.68–0.89; $p < 0.001$). The isolated discrimination powers of MELD-Na and CRP were better when applied to the subpopulation of patients with ACLF [MELD-Na with a discrimination power of 0.95 (CI95% 0.01–1.00; $p = 0.001$) and 0.94 (CI95% 0.01–1.00; $p = 0.001$) for IPM and M3, respectively and CRP with a discrimination power of 0.82 (CI95% 0.01–1.00; $p = 0.02$) and 0.79 (CI95% 0.57–1; $p = 0.33$) for IPM and M3, respectively]. However, there were no advantages in their association in a single model [discrimination power of 0.93 (CI95% 0.01–1.00; $p = 0.002$) for IPM and 0.94 (CI95% 0.01–1.00; $p = 0.001$) for M3].

**Conclusion:** CRP has a prognostic value in patients with decompensated cirrhosis, and it's an easily accessible tool. However, it doesn't appear to add any value to the predictive model MELD-Na.

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All other authors have declared no conflicts of interest.

## P1123 ACUTE-ON-CHRONIC LIVER FAILURE - A DYNAMIC SYNDROME

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**Introduction:** Acute-on-chronic liver failure (ACLF) is a recently defined syndrome characterized by an acute decompensation of cirrhosis with organic failure (s) and high mortality.[1] It is a dynamic syndrome that changes over time and should be assessed repeatedly. It is not clear whether there is a time point that correlates best with prognosis.[2]

**Aims & Methods:** Retrospective unicentric study including patients admitted for acute decompensation of cirrhosis between January/14 and December/15 that fulfilled ACLF criteria, at admission or during hospitalization. Patients were characterized at ACLF onset, at 48 h, 3 to 7 days and at the last available assessment in the first 28 days. 28-day (M28) and 90-day mortality (M90) were calculated.

**Results:** 38 patients (age $62.0 \pm 10.0$ years; 89.5% male) fulfilled ACLF criteria, at admission (50.0%) or during hospitalization. ACLF grades were: ACLF1 63.2%, ACLF2 23.7%, ACLF3 13.2%. 18 patients (47.4%) were admitted in an intensive care unit. ACLF resolved or improved in 62.2%, had a steady or fluctuating course in 13.5% and worsened in 24.3%. Resolution was observed in 58.3% ACLF1, 55.6% ALCF 2 and 25.0% ACLF3. Patients with ACLF resolution had lower M28 (10.0% vs 82.4%, $p < 0.0001$) and M90 (45.0% vs 88.2%, $p = 0.006$). Patients who developed ACLF during hospitalization had higher M28 (63.2% vs 26.3%, $p = 0.022$) and M90 (84.2% vs 47.4%, $p = 0.017$) than patients with ACLF at admission. Despite not reaching statistical significance, final ACLF grade was superior to the initial grade predicting M28 (AUROC $0.882 \pm 0.070$ vs $0.655 \pm 0.090$, $p = 0.09$) and M90 ($0.742 \pm 0.687$ vs $0.645 \pm 0.0745$, $p = 0.45$); the final CLIF-OF (CLIF Organ Failure) score was also superior to the initial score predicting M28 (AUROC $0.968 \pm 0.0267$ vs $0.800 \pm 0.0802$, $p = 0.05$) and M90 ($0.927 \pm 0.0418$ vs $0.765 \pm 0.0760$, $p = 0.06$).

**Conclusion:** In our population, prognosis was better defined by the early course of ACLF than by the initial evaluation, illustrating the dynamic nature of this syndrome.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1124 CLINICAL PROFILE OF PATIENTS WITH HEPATITIS E

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**Introduction:** Hepatitis E is an important cause of acute viral hepatitis in India.[1] The disease is usually self limited and has a case fatality rate of $<0.1\%$ in general population. However it is more severe, amongst pregnant women and often lead to fulminant hepatic failure and death in a significant proportion of patients.[2]HEV is a positive sense single stranded RNA icosahedral virus with a 7.5 kilobase genome classified under the genus Hepevirus.[3] Transmission is fecoral. Epidemic occurance is common. According to the South-East Asia Regional Office of the World Health Organization (WHO), hepatitis E is widespread in developing countries, accounting for upto 60–70% of all sporadic cases of acute viral hepatitis.[1,4] HEV causes high mortality in pregnant women, 20–30% as compared to 0.2–1% in general population.[5,6]

**Aims & Methods:** This study was conducted over a period of 5 years from Jan 2010 till Dec 2015. This was a retrospective observational study. All the patients tested positive for anti HEV IgM antibodies were included in the study including pregnant women, children and patients with preexisting Chronic Liver Disease. Details of clinical history at presentation to the hospital, history of pre existing Chronic Liver Disease, clinical examination, Investigation reports, Progression of the disease, response to treatment, complications encountered and outcome of the disease were noted.

**Results:** Males were more affected than females in all the age groups. The highest incidence was found in the age group of $>51$ yrs. Three out of the fifteen females were pregnant on admission. Twenty three (31.5%) patients amongst the seventy three had preexistent chronic liver disease. A majority of the patients presented with jaundice (91.78%). Other associated symptoms in the decreasing order of frequency were – anorexia (78.08%), nausea/vomiting (68.49%), abdominal pain (58.90%), sleep disturbances (49.31%) and hepatomegaly (50.68%). Pruritis, bleeding manifestations and altered consciousness were present in 23.28%, 20.54% and 16.43% of patients, respectively Serum Bilirubin values were elevated in all the patients with the lowest value noted at 1.5 mg/dl and the highest value noted was 41.2 mg/dl. ALT raise was seen in 84.12% patients. The highest value noted was 7355 U/L. Hepatic coagulopathy was the commonest complication (34.24%). Renal failure was noted in 16.43%, hepatic encephalopathy in 13.69% and fulminant hepatic failure in 7.93% respectively. There were no deaths among the general population. Overall mortality was 5 patients (6.84%) and all of them had background history of CLD. There were no deaths among pregnant women in the study nor were any cases of Intra Uterine Deaths. Among 23 patients with CLD, 21 patients (91.30%) had ACLF with mortality of 5 amongst them.

**Conclusion:** We concluded that acute viral hepatitis E is generally a self limiting disease among the general population, but can cause significant morbidity and mortality among special groups (pregnant women and people with preexisting Chronic Liver Disease). Progression of HEV related illness depends on multiple factors like age, comorbid illnesses, nutritional status, initial severity at presentation, early diagnosis, timely intervention and effective treatment.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1125 KERATIN VARIANTS ASSOTIATED WITH LIVER DISEASE CAUSED BY HBV IN CHINESE PATIENTS

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**Introduction:** Hepatitis B Virus infection is a common chronic liver disease characterised by familial aggregation in Chinese population in which host genetic factors may be involved. Keratin serves as a cytoskeleton that protects the liver from injuries and its mutations lead or predispose to the development of multiple liver diseases.

**Aims & Methods:** This study is to explore the characteristic of keratin variants in Chinese patient with liver disease caused by HBV. Our research has sequenced the entire coding regions and exonic-intronic boundaries of Keratin 8 and 18 with Sanger method that were amplified by polymerase chain reaction from blood DNA of HBV group and matched control group in the First Affiliated Hospital of Sun Yat-sen University from January 2009 to December 2015. HBV serologic indicators, HBV DNA levels, liver function, blood cells count and imaging examination were assessed.The relation among HBV infection, disease severity and keratin mutation was assessed by chi-square test. Conservation analysis of Keratin mutation firstly discovered in our study was performed with Clustal X software.

**Results:** Of the 713 examined subjects, 174 cases were diagnosed with chronic hepatitis B (CHB), while 192 cases with hepatitis B associated liver decompensated cirrhosis (HBDLC) and 174 cases with primary liver carcinoma (PLC). The frequency of mutations including missense mutation and intron mutation at keratin in study group was significantly higher than that of control group (8.15% vs 0.58%, respectively, $p = 3.66*10\,E\text{-}6$). Additionally, there was a trend toward an increase in both missense mutation and intron mutation in the study group as compared with control group (3.89% vs 0.58%, $p = 0.03$, 4.26% vs 0%, $p = 0.045$). Significant statistics difference was found between CHB group and control in multiple comparison (6.32% vs 0.58%, $p = 0.006$), except HBDLC and PLC. 21 missense mutations (3.89%) were found in study group, and K8 R341H constituted the most frequent amino acid-altering variant found. We also detected four novel and hitherto undescribed amino acid-altering variants (K8R469C, K8R469H, K8 A447V, K8K483T). Multiple sequence comparison analysis revealed that all novel K8 variants were at conserved site except for K8 A447V. In CHB subgroup, both of the HBV DNA levels and median model for end-stage liver disease (MELD) score were higher in those with missense mutation than that of without. But we did not find differences in positive HBV family history rates between the mutation patients and those without. Both HBV aggregation family and control group exhibited similar rates of mutations.

**Conclusion:** Keratin serves as a predisposing factor in exacerbation of CHB, but may not be linked to HBV familial aggregation.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1126 ASSOCIATION OF INTERLEUKIN 28B SINGLE NUCLEOTIDE POLYMORPHISMS WITH THE SUSCPTIBILITY OF HEPATITIS C VIRUS INFECTION IN EGYPTIAN POPULATION. A MULTICENTRE FAMILY BASED ASSOCIATION STUDY

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**Introduction:** Approximately 25% of infected individuals with acute HCV will spontaneously resolve HCV infection, developing robust protective immunity against reinfection while the remaining 70% of those individuals will develop chronic infection. Recently, genome-wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) near the IL28B gene (encoding IFN-λ3) to be strongly associated with the spontaneous and treatment-induced viral clearance.

**Aims & Methods:** The aim of this work to show the possible association of IL-28B with HCV infection outcome. Five SNPS spanned on 14 kb in promoter region of IL28B gene were genotyped by real time PCR using TaqMan allelic discrimination kit (Applied Biosystems, Foster City, CA, USA) according to the manufacturer's protocol. A total 230 families (985 subjects) from upper & lower Egypt (east & west delta), we compared the risk of allele carriage of selected markers in different groups. These groups included spontaneous clearance (n108), chronic HCV patients (n397), and negative control (n480) individuals. Genotyping of five SNPs (rs12980275, rs8105790, rs12979860, rs8099917 and rs10853728) near the IL28B region was performed.

**Results:** Across the different markers the allele carriage of wild alleles was significantly higher in in spontaneous clearance compared to that in chronic. The peak of significant results obtained with T allele of SNP rs 8099917 (OR = 0.3307, 95% CI 0.1917 to 0.5703, P = 0.0001) and extended across the C allele of rs 1297860 (OR = 0.6004.95% CI 0.4328 to 0.8329 P = 0.0022), T allele of rs 8105790 (OR = 0.7336, 95% CI 0.3692 to 0.7837, P = 0.0012) and A allele of rs 12980275 (OR = 0.7458.95% CI 0.5803 to 0.9275, P = 0.0035) then the significant result disappear at rs 10853728 (G/C).This indicates that T allele of rs 8099917 SNP of IL28B gene polymorphism may have crucial role in spontaneous viral clearance of HCV infection. However, the allele carriages of mutant alleles of different SNPs were significantly higher in chronic HCV group compared to that of negative control group. The peak of results was observed with allele T of SNPrs 1297860 (OR = 1.758, 95% CI 1.4812 to 1.991, P < 0.0001) and extended along the C allele of rs 8105790 (OR = 1.5369, 95% CI 1.1812 to 1.7991, P = 0.0096), G allele of rs 12980275 (OR = 1.5069, 95% CI 1.4812 to 1.7991, P = 0.0009) and C allele of rs 10853728 (OR = 1.3569, 95% CI 1.0912 to 1.6689, P = 0.0052). This indicates that T allele of rs 1297860 SNP of IL28B gene polymorphism may have crucial role in persistence of HCV infection. Furthermore it was found that spontaneous clearance of HCV was associated with the carriage of protective haplotype ATCTG, While the chronic HCV was associated with carriage of the haplotype GCTGC.

**Conclusion:** Spontaneous clearance of HCV was associated with the wild allele carriage with the peak at T allele of rs 8099917 SNP of IL28B gene and with the carriage of protective haplotype ATCTG, While the chronic HCV was associated with T allele of rs 1297860 SNP & with the carriage of the haplotype GCTGC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1127 SERUM AUTOTAXIN CAN PREDICT LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B VIRUS INFECTION

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**Introduction:** Serum autotaxin (ATX) is originally isolated from the conditioned medium of human melanoma cells as a stimulator of cell migration, but it is reported to be a highly reliable, non-invasive marker of liver fibrosis in patients with hepatitis C virus infection[1] or cirrhosis[2].

**Aims & Methods:** We assessed the ability of serum ATX to diagnose liver fibrosis in patients with chronic hepatitis B virus (HBV) infection. Serum ATX levels were retrospectively evaluated in 101 treatment-naïve patients with HBV-related chronic hepatitis and cirrhosis who had undergone liver biopsy at our hospital.

**Results:** Consistent with a previous report[3], serum ATX exhibited gender differences. The correlations between ATX and other non-invasive markers (hyaluronic acid type IV collagen 7 S, WFA+-M2BP, APRI, FIB-4, serum albumin, and platelet count) and those markers indicating hepatitis activity (AST/ALT and histological activity) were stronger in men than in women. Serum ATX levels significantly correlated with liver fibrosis stages ($r = 0.524$ and $p = 0.0006$ in women; $r = 0.552$ and $p = 0.00001$ in men), and serum ATX proved to be the most reliable factor for accurately predicting significant fibrosis with an area under the receiver operating characteristic curve (AUROC) of 0.792 in men and 0.786 in women, when compared with all other non-invasive markers.

**Conclusion:** These results suggest that serum ATX can predict liver fibrosis with chronic HBV infection, although gender differences should be taken into consideration. This is the first study clarifying the clinical importance of serum ATX in HBV-infected patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1128 A PROSPECTIVE STUDY ON THERAPEUTIC EFFECTS OF SEQUENTIAL THERAPY IN PATIENTS WITH CHRONIC HEPATITIS B RESPONDING TO NUCLEOSIDE ANALOGUES

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**Introduction:** To date, there are few reports on therapeutic effects of sequential therapy (ST) with chronic hepatitis B responding to nucleoside analogues (NAs).

**Aims & Methods:** Patients who had achieved favorable therapeutic outcomes with long-term administration of NAs are prospectively being followed up by dividing them into those switching to ST and those continuing NA therapy, and we assessed therapeutic effects for up to 96 weeks from the start of follow-up. Thirty patients with chronic hepatitis B who achieved a HBsAg level below 2000 IU/mL and a hepatitis B virus (HBV) DNA level below 2.1 log copies (LC)/mL with long-term administration of NAs (median: 50 months) were divided into two groups: the ST group of 15 patients who consented to switching to ST and the NA group of 15 who continued NA therapy without consenting to ST. The therapeutic effects from the start of follow-up to 96 weeks were prospectively assessed. In the ST group, pegylated interferon (Peg-IFN) a-2 a was administered for 48 weeks, including 4 weeks of concomitant administration with NAs, after obtaining consent. Drug-free remission was defined as an alanine aminotransferase (ALT) level below 31 IU/L and an HBV-DNA level below 4.0 LC/mL.

**Results:** There were no differences in pretreatment patient characteristics between the ST and NA groups. At 96 week from the start of follow-up, all NA group patients maintained an ALT level below 31 IU/L and a HBV-DNA level below 2.1 LC/mL. On the other hand, in the ST group, 60% of patients achieved drug-free remission at 96 week (including those with complete remission defined as ALT < 31 IU/L and HBV-DNA < 2.1 LC/mL, accounting for 20%), whereas approximately 15%, with an ALT level of 31 IU/L or more and an HBV-DNA level of 4.0 LC/mL or more, required NA therapy resumption. Moreover, the patients who required NA therapy resumption had been unable to maintain hepatitis B core-related antigen (HBcrAg) levels below 3.0 log U/mL during Peg-IFN administration, and the levels rose to 4.0 log U/mL or more after ST completion. Regarding fluctuations in HBsAg levels, the median in the NA group was 689 IU/ml before treatment, 630 IU/mL at 48 week, 558 IU/mL at 72 week, and 554 IU/mL at 96 week, remaining essentially unchanged, whereas the respective median values in the ST group were 691, 458, 326, and 264 IU/mL, showing a significant decrease ($P < 0.05$). However, no patients showed HBsAg loss during follow-up. Interestingly, as HBV-DNA elevation and severe hepatic dysfunction were observed in one patient of ST group at 72 week, administration of NA was resumed. As a result, HBsAg levels markedly decreased (72w: 188 IU/mL, 96w: 0.13 IU/mL).

**Conclusion:** In patients who had achieved favorable therapeutic outcomes with long-term NA administration, administering ST decreased HBsAg levels, and the 96 weeks follow-up results showed that drug-free remission was achieved in 60% of these patients. In addition, based on the marked decrease in HBsAg levels in one case following acute exacerbation after ST completion, the adoption of ST is considered to be useful for lowering HBsAg levels.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1129 MAY "GILBERT'S-LIKE" SYNDROM BE PART OF SPECTRUM OF PERSISTENT UNCONJUGATED HYPERBILIRUBINEMIA IN POST-HEPATITIS PATIENT?

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**Introduction:** Following the effective treatment of acute and chronic liver diseases, the majority of patients in recovery of liver diseases present liver enzyme index declining to normal. However, it is not uncommon that persistent or intermittent mild unconjugated hyperbilirubinemia could be detected and hardly be eliminated. The UGT1A1 mutation has been claimed to lead to Gilbert syndrome (GS) and appears to be considerably different among ethnic groups.

**Aims & Methods:** To investigate the correlation between gene polymorphisms of bilirubin uridine diphosphate-glucuronosyltransferase (UGT1A1) and the development of unconjugated hyperbilirubinemia in clinical Gilbert's syndrome and posthepatitis hyperbilirubinemia. The blood samples of 294 patients, including 85 patients who were clinically diagnosed as Gilbert syndrome (GS), 70 patients who had indirect hyperbilirubinemia during the recovery period of chronic liver diseases, 109 patients with normal hepatic function and 21 active chronic hepatitis B patients as the hepatitis control group patients were collected. All samples were tested for the identification of UGT1A1 *28 and UGT1A1 *6 genotype by pyrosequencing technique. The total bilirubin and indirect bilirubin levels were measured. The frequency and the diverse UGT1A1 diplotypes formation were analyzed to evaluate the correlation between development of indirect hyperbilirubinemia and gene polymorphisms of UGT1A1. The data were presented as mean ± standard error of the means (SEM). Statistical analysis was performed by SPSS statistical software version 19.0 using either Chi-square, contingency table or Fisher's exact probability method depending on the dataset. A $p < 0.05$ indicated statistical significance.

**Results:** The gene variation of UGT1A1 *28 and UGT1A1 *6 were positively correlated to the level of serum bilirubin. Homozygous TA insertion in the TATA box of the promoter region (UGT1A1*28) (22%) and homozygous UGT1A1*6 (14%) were frequent in GS. There is no homozygous genotype for both UGT1A1*6 and UGT1A1*28 were detected in healthy control patient (UGT1A1*28: 0.465 vs 0.101; UGT1A1*6: 0.288 vs 0.142; $p < 0.05$). The allele gene frequency for UGT1A1*28 was significant elevated in GS comparing with healthy-control patients. Homozygous TA insertion in the TATA box of the promoter region (UGT1A1*28) (14%) and homozygous UGT1A1*6 (11%) were frequent in GS. There is no homozygous genotype for both UGT1A1*6 were detected in hepatitis control patient. And homozygous genotype for UGT1A1*28 was only found in one hepatitis control patient. The allele gene frequency for UGT1A1*28 was significant elevated in post-hepatitis comparing with hepatitis-control patients (UGT1A1*28: 0.350 vs 0.143; UGT1A1*6: 0.286 vs 0.119; $p < 0.05$). The polymorphosim of UGT1A1 present similar patten in GS and post hepatitis hyperbilirubinemia patients.

**Conclusion:** Gene polymorphisms of UGT1A1*28/*6 in patients who had indirect hyperbilirubinemia during the recovery period of chronic liver diseases present similar pattern as GS patient. The "Gilbert's-like" syndrom might be part of spectrum of persistent unconjugated hyperbilirubinemia in post-chronic hepatitis patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1130 DIABETES MELLITUS AND NOT HEPATIC STEATOSIS ALONE INCREASE THE RISK OF ADVERSE EVENTS IN PATIENTS WITH CHRONIC HEPATITIS B

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**Introduction:** Chronic Hepatitis B (CHB) remains an important disease in many parts of the world and with the rising prevalence of metabolic syndrome worldwide, patients with concomitant CHB and hepatic steatosis are increasingly encountered. However the characteristics, interaction and long-term follow-up in these patients remain to be elucidated.

**Aims & Methods:** Aim. To assess the liver histology, clinical characteristics and progression to cirrhosis and hepatocellular carcinoma (HCC) in CHB patients with or without concomitant hepatic steatosis. Methods. 182 CHB patients with liver biopsy performed between 2000–2006 were identified from hospital records. Liver biopsy histology was reviewed for presence of >5% steatosis and non-alcoholic steatohepatitis (NASH). The clinical characteristics were analysed and stratified by presence (Group 1) or absence (Group 2) of hepatic steatosis. Patients were prospectively followed-up for development of Hepatocellular carcinoma (HCC) or new cirrhosis in patients with low fibrosis score till 1/04/2016. HCC was confirmed based on contrast enhanced imaging. Cirrhosis was defined based on fibroscan or liver histology or at least two of the three ultrasound findings i.e nodular liver, irregular margins or caudate lobe hypertrophy.

**Results:**

Baseline characteristics

| | Group 1 (Hepatic steatosis) N = 100 | Group 2 (no steatosis) N = 82 | p value |
|---|---|---|---|
| Age in years | 44.5 ± 11.1 | 41.4 ± 14.1 | 0.09 |
| Gender (% males) | 77.0 | 65.8 | 0.07 |
| HBV DNA in log copies/ml | 7.15 ± 1.64 | 7.46 ± 1.40 | 0.18 |
| ALT in IU/L | 155 ± 216 | 183 ± 252 | 0.35 |
| Bilirubin in μmol/l | 17.65 ± 12.9 | 20.83 ± 33.8 | 0.39 |
| Albumin | 39.5 ± 4.8 | 40.62 ± 22.6 | 0.628 |
| Diabetes Mellitus in % | 16.5% | 6.1% | 0.025 |

Hepatic steatosis was seen in 54.9% (100/182) of patients with hepatitis B on biopsy. At the time of biopsy the mean age was 43.1 ± 12.5 years with 72.0% males, predominantly of Chinese ethnicity (94.5%). Baseline characteristics are shown in table 1. Cirrhosis was seen in 19/100 in Gp1 and 21/82 in Gp 2 at baseline. On mean follow-up of 10.6 ± 3.8 years, hepatocellular carcinoma was seen in 12/100 subjects in Gp1 and 7/82 in Gp 2 ($p = 0.28$). HCC was seen in 12/99 in Gp1 and 7/83 in Gp 2 ($p = 0.29$). However on cox-regression analysis for HCC risk factors, Diabetes Mellitus (HR 4.4, CI 1.97–13.7 $P = 0.002$), Age

($p < 0.001$) were significant risk factors for development of HCC. Hepatic steatosis was not a significant risk factor for HCC on cox-regression analysis ($p = 0.18$) New cirrhosis was seen in 20/81 in Gp1 and 18/62 in Gp 2 ($p = 0.56$). Age was significantly different in the patients who progressed to cirrhosis ($p = 0.02$), while Diabetes Mellitus (DM), Fatty liver, ALT were not significant. In the subgroup of patients with low HBV DNA (< 6 log copies/ml) and low Ishak fibrosis score (< 4) 31 patients were identified. Progression to cirrhosis was seen in 3 of 22 patients in Gp 1 and none of the patients in group 2. Diabetes mellitus and advanced age being significant risk factors (with $p = 0.045$ and 0.04 respectively) with HR of 19.6, CI 1.18–333.0 for DM on cox-regression analysis

**Conclusion:** In patients with Hepatitis B presence of concomitant steatosis does not increase the risk of hepatocellular cancer development but Diabetes mellitus remains a risk factor. However in patients with low viral load and early fibrosis, presence of diabetes mellitus remains independent risk factor for progression to cirrhosis and not hepatic steatosis alone.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1131 EARLY DECREASE OF LIVER STIFFNESS AFTER INITIATION OF ANTIVIRAL THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C INDICATES THAT LOWER CUT-OFF VALUES FOR LIVER STIFFNESS ARE APPROPRIATE FOR MONITORING LIVER FIBROSIS AFTER INITIATION OF ANTIVIRAL TREATMENT


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**Introduction:** Liver elastography is widely used to assess liver fibrosis in patients with chronic hepatitis C and has also been recommended to monitor liver fibrosis after successful antiviral therapy. We studied early changes of liver stiffness after initiation of antiviral treatment.

**Aims & Methods:** The study population comprised 53 patients with chronic hepatitis C (mean age: $49.4 \pm 10.7$; METAVIR fibrosis stage F2, n = 23; F3, n = 12; F4, n = 18; genotype (GT), n = 32; GT3, n = 17; GT4, n = 4; mean BMI: $25.1 \pm 3.8$). All patients were treated with interferon-free regimens. Prior to therapy and 1–6 weeks after initiation of antiviral treatment fibrosis stage was assessed by transient elastography using the Fibroscan® 502 Touch device. Cut-off values for liver stiffness were defined as 7.1 kPa for $F \geq 2$, 9.5 kPa for $F \geq 3$ and 12.5 kPa for F = 4. Only procedures with 10 successful measurements of liver stiffness with an interquartile range < 30% were considered reliable.

**Results:** Mean liver stiffness at baseline was $14.69 \pm 11.15$ kPa and decreased to $12.41 \pm 9.83$ kPa at week 1–6 ($p = 0.006$). When the same Fibroscan® cut-off values applied at baseline were applied after initiation of antiviral therapy the following results were obtained: Within 6 weeks after initiation of treatment fibrosis stage improved by at least one stage in 23/53 (43%) patients, remained stable in 28/53 (53%) and worsened in 2/53 (4%). Decrease of liver stiffness did not correlate with baseline AST ($r = 0.28$) or ALT ($r = 0.04$) levels.

**Conclusion:** After initiation of antiviral therapy a significant decrease of liver stiffness can be observed within 6 weeks, probably caused by resolution of inflammation. Our data clearly indicate that lower cut-off values for liver stiffness are appropriate for monitoring liver fibrosis after initiation of antiviral therapy.

**Disclosure of Interest:** M. Gschwantler: Michael Gschwantler received speaking fees and participated in advisory boards for Janssen, Abbvie, MSD, BMS and Gilead Sciences
All other authors have declared no conflicts of interest.

### P1132 REAL LIFE EXPERIENCE WITH DIRECT ACTING ANTIVIRALS IN THE MANAGEMENT OF HCV PATIENTS WITH REDUCED FUNCTIONAL HEPATIC RESERVE


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**Introduction:** Treatment of HCV showed a remarkable change recently. Many direct acting antiviral (DAA) drugs are introduced as Sofosbuvir which is a pangenotypic HCV NS5B nucleotide polymerase inhibitor. It has been tried both as dual therapy with ribavirin or simeprevir and also as a part of triple therapy which included pegylated interferon alfa and ribavirin. High rates of SVR have been theoretically shown with a postulated safety profile both in cirrhotic and noncirrhotic patients. Patients with decompensated cirrhosis mostly will not benefit from HCV antiviral therapy even if HCV-RNA became negative, as they reached a point of no return. Many patients with apparently adequate liver function tests and Child Pugh score may not sustain combined antiviral therapy due to development of complications and this may need the development of a practical index.

**Aims & Methods:** Assessing the efficacy, safety of direct acting anti virals in a cohort of Egyptian patients presented with occult reduction in functional hepatic reserve. Patients were included if they had chronic active HCV proved by positivity of HCV RNA and elevated transaminases. the functional hepatic reserve was predicted by a model composed of defined cutoff values: AST to platelet count ratio (APRI) + Caudate/right lobe ratio + prothrombin concentration (PC) in points. APRI score with the selected cut-off value of 1.The cutoff value of Caudate/right lobe ratio (C/RL) was 0.66, Prothrombin concentration (PC) is a sensitive prognostic indicator. According to PC, the patient is given a score as follows; PC > 80% → 0, PC: 70–79% → 1, PC: 60–69 → 2, PC: 50–59 → 3, PC < 50→ 4. 300 patients with chronic active HCV (275 M, 125 F) were evaluated and enrolled if their functional hepatic reserve score (FRS) was more than 3.66; in the period from January 2015 till October 2015. they were subclassified into: **(Dual therapy):** (n = 200), 30 patients received simeprevir and sofosbuvir for 3 months and 170 patients received ribavirin and sofosbuvir for 6 months. **(Triple therapy):** (n = 100) who received Sofosbuvir plus peginterferon and ribavirin for 12 weeks.

**Results: (Dual therapy):** Complications occurred in 120 patients (60%, functional hepatic reserve score (FRS) $4.06 \pm 0.5$) mainly anaemia (80 patients, 66.7%), ascites (34 patients, 28.3%), GIII hyperbilirubinemia mainly direct (89 patients, 74.2%), photosensitivity in 14 patients (11.7%), hepatic encephalopathy (HE) (20 patients, 16.7%), accidental diagnosis of HCC near the end of treatment in 10 patients (8.3%); 130 patients showed SVR (65%, FRS mean value $3.55 \pm 0.4$), 70 patients developed virological relapse (35%, FRS: $3.88 \pm 0.5$) **(Triple therapy):** Complications occurred in 61 patients (61%, FRS: $3.78 \pm 0.3$) mainly anaemia (51 patients,83.6%), jaundice GII-III mainly indirect bilirubin (43 patients, 70.5%), ascites in 12 (19.7%), HE in 8 (13.1%). 86 patients (86%) achieved end of treatment response, 75 patients achieved SVR (75%, FRS mean value $2.9 \pm 0.7$), 25 patients showed relapse of viremia (25%, FRS: $3.79 \pm 0.3$).

**Conclusion:** In real life, SVR with DAAs in dual therapy is 65% and 75% in triple therapy in patients with reduced functional hepatic reserve with FRS more than 3.66.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1133 FEASIBILITY OF ELASTOGRAPHIC METHODS IN ASSESSING SPLEEN STIFFNESS IN PATIENTS WITH HCV COMPENSATED LIVER CIRRHOSIS


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**Introduction:** The aim of this study was to compare the feasibility of four ultrasound based elastographic methods used for assessing spleen stiffness.

**Aims & Methods:** The study included 42 subjects diagnosed with HCV compensated liver cirrhosis in whom spleen stiffness (SS) was evaluated in the same session by means of 4 elastographic methods: 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) and the LogiqE9, General Electric (2D-SWE GE). All examinated patients (n = 42) presented splenomegaly defined by values higher than 12.5 cm. Reliable SS measurements were defined as follows: for ElastPQ, VTQ and 2D-SWE.GE- the median value of 10 SS measurements with a success rate ≥60% and an interquartile range < 30% and for 2D-SWE the mean value of 3 measurements acquired in a homogenous area. SS was expressed in kPa for 2D-SWE, ElastPQ and in m/s for VTQ and 2D-SWE GE.

**Results:** Reliable SS measurements were obtained in: 85.7% with 2D-SWE.GE, 85.7% with VTQ, 47.61% with 2D-SWE and 30.95% with ElastPQ. 2D-SWE

GE and VTQ had similar rates of reliable SS measurements. The mean value for 2D-SWE GE was 2.46 ± 0.74 m/s and for VTQ was 3.14 ± 0.58 m/s.
**Conclusion:** 2D-SWE GE and VTQ were the most feasible shear-waves elastographic methods in assessing spleen stiffness in patients with HCV compensated liver cirrhosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1134 DIRECT ACTING ANTIVIRALS FOR CHRONIC HEPATITIS C GENOTYPE 3: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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**Introduction:** Although the introduction of direct acting antivirals (DAAs) improved efficacy of chronic hepatitis C virus (CHC) treatment significantly, results in CHC genotype 3 remain suboptimal. There are several treatment options available, but head-to-head studies are the exception.
**Aims & Methods:** We aimed to (1) perform a systematic review and network meta-analysis to indirectly compare efficacy (sustained virological response, SVR) of DAAs in CHC genotype 3; (2) assess the role of ribavirin, length of therapy and presence of cirrhosis on treatment efficacy. We conducted a systematic search in the Pubmed, EMBASE and Web of Science databases (Jan 2004–Mar 2016). We performed a Bayesian network meta-analysis using a random effects model to indirectly compare identified regimes (R and Winbugs). Data per regime is presented as mean chance on SVR and 95% credibility interval (95%CrI). Effect of ribavirin, extension of treatment and cirrhosis are presented as odds ratio (OR) with 95%CrI.
**Results:** Our search identified 3261 articles. A total of 19 studies (2998 patients in 29 different treatment regimes) met inclusion criteria. Some 1673 (56%) patients were treatment naïve and 497 (17%) were cirrhotics. The numerically highest chance on SVR were estimated for the regimes sofosbuvir/velpatasvir with ribavirin for 12 weeks (98.4%, 95%CrI 96.1–99.5) or without ribavirin for 24 weeks (98.7%, 95%CrI 96.5–99.7). For other regimes the chances of SVR were numerically lower, but 95%CrIs overlapped: sofosbuvir/daclatasvir with ribavirin for 12 (84.1%, 95%CrI 59.9–96.3), 16 (92.4%, 95%CrI 78.1–98.5) or 24 (95.5%, 95%CrI 86.5–99.2) weeks or without ribavirin for 24 weeks (86.6%, 95%CrI 63.9–97.4), sofosbuvir with peginterferon and ribavirin for 12 weeks (92.9%, 95%CrI 84.5–97.5), and sofosbuvir/velpatasvir for 12 weeks (94.8%, 95%CrI 89.0–98.2). For the added value of RBV, we found an OR of 3.53 (95%CrI 2.00–5.89), and an OR of 4.57 (95%CrI 2.52–7.76) for extension of therapy from 12 to 24 weeks, and an OR of 0.76 (95%CrI 0.39–1.35) for the effect of cirrhosis on SVR.
**Conclusion:** This indirect comparison of treatments using Bayesian network meta-analysis reveals that sofosbuvir /velpatasvir with ribavirin for 12 or without ribavirin for 24 weeks in CHC genotype 3 patients is the best option. However, this was not significantly higher than the currently available regimes for genotype 3. Our analyses suggest that both ribavirin and extension for treatment have an additional value in obtaining SVR, while cirrhosis did not significantly affect SVR. Choice of treatment may depend on factors such as patient characteristics, risk of adverse events and price of therapy.
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All other authors have declared no conflicts of interest.

## P1135 EFFECT OF HEPATITIS C TREATMENT WITH DIRECT-ACTING ANTIVIRALS ON VITAMIN D IS DEPENDENT ON SEASONALITY

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**Introduction:** Hypovitaminosis D is very common in chronic infection with hepatitis C virus (HCV), and is possibly due to viral effects on 25-hydroxylation and/or lipid metabolism. On the other hand, vitamin D levels vary according to sun exposure, which is necessary to its endogenous synthesis. Vitamin D has antifibrotic effects and modulates immune responses, and therefore its deficiency may be implicated in the pathogenesis of liver disease.
**Aims & Methods:** We aim to characterize the impact of treatment of hepatitis C with direct-acting antivirals without interferon (DAA) on vitamin D levels.
Analysis of all patients with chronic hepatitis C treated with DAA at one center, with serum 25-hydroxycholecalciferol levels prospectively performed on first day of therapy (baseline), end-of-treatment (EOT) and/or 12 weeks after end-of-treatment (PT12). Patients with detectable viral load on PT12 were excluded. Vitamin D deficiency was defined as $<20$ ng/mL (according to Endocrine Society). Year months were classified as "sunny" vs "non-sunny", if sun hours were $\geq 8$ (April-September) vs $<8$ (October-March) respectively, according to data on http://www.weatheronline.pt for Lisbon. Patients were treated according to national and/or EASL recommendations. Statistical analysis performed with STATA®v12.1 and Excel®2010.
**Results:** Fifty-five patients were analyzed, 72.7% (40/55) males, median age 57 (41;78) years. All patients were treated with sofosbuvir/ledipasvir, with or without ribavirin, during 12 or 24 weeks, and had viral load $<15$UI/mL on EOT. Treatments were initiated between April and October 2015. Thirty-two patients had HCV genotype 1, 19 had HCV genotype 3 and 4 had HCV genotype 4. On baseline, 63.6% (35/55) of patients had vitamin D deficiency. Globally, mean vitamin D levels decreased from baseline to EOT (18.8 ng/mL to 14.5 ng/mL; $p < 0.01$; $n = 55$) and then further declined from EOT to PT12 (16.1 ng/mL to 13.1 ng/mL; $p < 0.01$; $n = 27$). Among patients who completed therapy on "sunny" months ($n = 6$), mean vitamin D levels increased from baseline to EOT (17.0 to 19.6 ng/mL; $p = 0.35$; $n = 6$), and then decreased from EOT to PT12 (21.0 ng/mL to 15.3 ng/mL; $p = 0.13$; $n = 4$). Among patients who completed therapy on "non-sunny" months ($n = 49$), mean vitamin D levels decreased from baseline to EOT (19.0 ng/mL to 13.9 ng/mL; $p < 0.01$; $n = 49$), followed by a further decrease from EOT to PT12 (15.3 ng/mL to 12.8 ng/mL; $p < 0.01$; $n = 23$).
**Conclusion:** The impact of seasonality seems to override a possible effect of elimination of hepatitis C virus on vitamin D levels.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1136 FERROKINETICS, CALCIUM, VITAMIN D2 AND RED BLOOD CELL INDICES, DO THEY PREDICT CIRRHOSIS ON LIVER BIOPSY AND NON-RESPONSE TO ANTIVIRAL TREATMENT IN CHRONIC HEPATITIS C?

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**Introduction:** There is limited literature on the role of iron indices, calcium, vitamin D2 levels and red blood cell (RBC) indices in predicating fibrosis stages and anti viral treatment (AVT) response in chronic hepatitis C (CHC).
**Aims & Methods:** Aim: To correlate pre-treatment serum iron indices, RBC indices [mean platelet volume (MPV), red cell distribution width (RDW) and RDW/platelet count index (RPI) ], calcium and vitamin D2 levels with cirrhosis on liver biopsy (LB) and AVT response in CHC. Methods: We analyzed data of 1602 patients (January 2002 -July 2014) with CHC who underwent LB (Scheuer staging) and received AVT (pegylated interferon and ribavirin). Pre-treatment baseline parameters including serum iron indices, calcium, vitamin D2 levels and RBC indices were correlated with LB fibrosis stages and response to AVT.
**Results:** The mean age of the patients was 41.8 ± 9.6 years (1,365 males), the most common genotype was genotype-4 (65.6%). LB results showed stage-0 fibrosis in 1.9%, stage-1 in 32.9%, stage-2 in 39.5%, stage-3 in 19%, and stage-4 (cirrhosis) in 6.6% of the patients. On univariate analysis (UVA) high iron ($p < 0.001$), high ferritin ($p < 0.001$), high transferrin saturation ($p = 0.001$), high MPV ($p = 0.01$), high RPI ($p < 0.001$) correlated with cirrhosis on LB. On UVA, high serum iron levels ($p < 0.001$), high serum ferritin ($p < 0.001$), low vitamin D ($p = 0.036$) and high RPI (0.02) correlated with non-response to AVT. However none of these were independent predictors on multivariate analysis (MVA). On MVA, albumin (adjusted odds ratio, AOR = 0.84, CI = 0.74–0.91, $p = 0.001$), AST (AOR = 1.015, CI = 1.008–1.022, $p = 0.001$) and platelet count (AOR = 0.98, CI = 0.974–0.989) correlated with cirrhosis on LB. We derived a study score [8.5 -0.2(albumin, g/dL) + 0.01(AST, IU/L) - 0.02(platelet count, $10^9$/dL) ], which at a cut-off of > 4.7 had a predictive accuracy of 0.86 (95% CI- 0.83–0.90) for cirrhosis. Similarly on MVA; age (AOR = 1.036, CI = 1.007–1.065, $p = 0.01$), ALT (AOR = 0.990, CI = 0.984–0.996, $p = 0.002$), gamma-glutamyl transpeptidase (AOR = 1.012, CI = 1.007–1.017, $p < 0.001$) and platelet count (AOR = 0.989, CI = 0.984–0.995, $p < 0.001$) predicted non-response to AVT. We derived a study score [ (0.072 + 0.035(age, years) - 0.01(AST, IU/ml) + 0.01(GGT, IU/ml) - 0.01(platelet count, $10^9$/dL) ], which at a cut-off of 0.32 had a predictive accuracy of 0.748 (95% CI = 0.708–0.789) for non-response to AVT.
**Conclusion:** Iron indices and RDW/platelet index correlated with cirrhosis on liver biopsy and non-response to antiviral treatment on univariate analysis. However, only AST, albumin and platelet count were independent predictors of cirrhosis. Age, GGT, AST and platelet count were independent predictors of non-response to antiviral therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1137 REAL-LIFE SIDE EFFECTS OF INTERFERON-FREE THERAPY (OMBITASVIR / PARITAPREVIR / RITONAVIR + DASABUVIR +RIBAVIRIN) AND END OF TREATMENT RESULTS IN PATIENTS WITH COMPENSATED HCV CIRRHOSIS

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**Introduction:** Recently (November 2015), Interferon-free therapy became available in Romania only to patients with compensated HCV liver cirrhosis. The

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Demographic characteristics of the studied participants

| Group | HALT-C < 0.2 (n = 17) Group 1 | HALT-C ≧ 0.2 and ≦ 0.5 (n = 36) Group 2 | HALT-C > 0.5 (n = 13) Group 3 | Total (n = 66) | p value |
|---|---|---|---|---|---|
| Age, y | | | | | 0.001 |
| Range (all) | 22–65 | 31–79 | 50–74 | 22–79 | |
| Mean +/- SD (all) | 45.1 +/- 12.6 | 53.8 +/- 12.2 | 62.5 +/- 7.8 | 53.3 +/- 12.9 | |
| mean (women) | 48.1 +/- 13.5 | 54.3 +/- 10.5 | 64.2 +/- 8.1 | 54.7 +/- 12.0 | |
| Men, n (%) | 7 (41.2%) | 16 (44.4%) | 5 (38.5%) | 28 (42.4%) | 0.929 |
| pre-menopause, n (%) | 3 (17.6%) | 6 (16.7%) | 0 (0%) | 9 (13.6%) | |
| post-menopause, n (%) | 7 (41.2%) | 14 (38.9%) | 8 (61.5%) | 29 (43.9%) | 0.221 |
| Duration of menopause | | | | | 0.051 |
| Range | 1–15 | 3–26 | 3–28 | 1–28 | |
| Mean +/- SD | 5.29 +/- 4.89 | 12.79 +/- 7.88 | 14.88 +/- 8.85 | 11.55 +/- 8.2 | |
| Smoking | 4 (30.8%) | 6 (19.4%) | 1 (8.3%) | 11 (19.6%) | 0.383 |
| Drinking | 1 (8.3%) | 1 (3%) | 2 (16.7%) | 4 (7%) | 0.291 |
| HCV genotype | | | | | 0.547 |
| 1 a | 2 (11.8%) | 2 (5.6%) | 0 | 4 (6.1%) | |
| 1 b | 7 (41.2%) | 19 (52.8%) | 7 (53.8%) | 33 (50%) | |
| 1 | 9 (53%) | 21 (58.4%) | 7 (53.8%) | 37 (56.1%) | |
| 2 a | 3 (17.6%) | 11 (30.6%) | 5 (38.5%) | 19 (28.8%) | |
| 2 b | 2 (11.8%) | 3 (8.3%) | 0 | 5 (7.6%) | |
| 2 | 5 (29.4%) | 14 (38.9%) | 5 (38.5%) | 24 (36.4%) | |
| concurrent 1 b + 2 a | 3 (17.6%) | 1 (2.8%) | 1 (7.7%) | 5 (7.6%) | |
| Body mass index (kg/m$^2$) | 24.9 +/- 4.64 | 24.3 +/- 3.33 | 25.0 +/- 2.86 | 24.6 +/- 3.59 | 0.728 |
| Platelet level, ×1000/mm$^3$ | 227 +/- 47 | 168 +/- 36 | 116 +/- 54 | 173 +/- 57 | 0 |
| INR | 0.96 +/- 0.06 | 1.01 +/- 0.07 | 1.14 +/- 0.09 | 1.02 +/- 0.09 | 0 |
| Creatinine level, mg/dL | 0.77 +/- 0.16 | 0.78 +/- 0.18 | 0.74 +/- 0.18 | 0.77 +/- 0.17 | 0.774 |
| AST level, U/L | 80.94 +/- 84.75 | 62.58 +/- 35.52 | 87.92 +/- 28.63 | 72.30 +/- 52.15 | 0.239 |
| ALT level, U/L | 152 +/- 177 | 97 +/- 89 | 93 +/- 37 | 111 +/- 113 | 0.21 |
| Bilirubin level, mg/dL | 0.44 +/- 0.16 | 0.64 +/- 0.31 | 0.75 +/- 0.28 | 0.62 +/- 0.29 | 0.01 |
| Ca, mg/dL | 9.5 +/- 0.36 | 9.4 +/- 0.37 | 9.4 +/- 0.81 | 9.4 +/- 0.48 | 0.726 |
| Phosphate level, mg/dL | 3.78 +/- 0.54 | 3.67 +/- 0.47 | 3.47 +/- 0.88 | 3.65 +/- 0.59 | 0.381 |
| Albumin level, g/Dl | 4.66 +/- 0.26 | 4.48 +/- 0.31 | 4.15 +/- 0.34 | 4.46 +/- 0.35 | 0 |
| Bone-specific alkaline phosphatase, U/L | 37 +/- 21 | 40 +/- 19 | 49 +/- 46 | 41 +/- 26 | 0.429 |
| iPTH (10–69 pg/ml) | 22.05 +/- 14.94 | 36.13 +/- 33.44 | 38.25 +/- 19.92 | 32.92 +/- 27.80 | 0.17 |
| CTX (ng/mL) | 0.19 +/- 0.13 | 0.22 +/- 0.16 | 0.23 +/- 0.14 | 0.21 +/- 5.70 | 0.78 |
| 25(OH)D, ng/mL | 20.29 +/- 6.07 | 22.29 +/- 6.39 | 21.01 +/- 1.90 | 21.52 +/- 5.70 | 0.466 |
| HCV RNA (IU/mL ×10$^6$) | 36.9 +/- 5.7 | 8.5 +/- 20.2 | 4.43 +/- 7.2 | 6.44 +/- 15.6 | 0.514 |
| APRI | 1.17 +/- 1.22 | 1.24 +/- 0.77 | 3.08 +/- 2.38 | 1.58 +/- 1.51 | 0 |

only regimen is the Ombitasvir / Paritaprevir / Ritonavir + Dasabuvir + Ribavirin association.

**Aims & Methods:** The aim of this study was to evaluate the real-life side effects occurring during Ombitasvir / Paritaprevir / Ritonavir + Dasabuvir +Ribavirin therapy in a group of such patients who started treatment in December 2015 - January 2016, as well as their response to therapy. Methods: We conducted a prospective study including 50 patients with compensated HCV cirrhosis, diagnosed by clinical, elastographic, biologic or pathologic criteria treated for 12 weeks with Ombitasvir / Paritaprevir / Ritonavir + Dasabuvir +Ribavirin regimen. Each patient had follow-up visits at two, four, eight and twelve weeks after treatment initiation. Biologic tests included total bilirubin, ALT, AST and hemoglobin. Subjective complaints of the patients were also recorded. Anemia secondary to the treatment was defined as a decrease in hemoglobin <12 g/dL in women and <13 g/dL in men, or with more than 1 g/dl as compared to baseline; jaundice was defined as an increase in total bilirubin >3 mg/dl, and cytolysis was defined as an increase in AST or ALT of at least 2 times as compared to baseline. End of treatment (EOT) response was evaluated by viral-load assessment by PCR. EOT response was defined as a viral load < 15 IU/ml.

**Results:** The group included 50 patients - mean age 60 ± 8 years, 58% (29) women, all of them genotype 1 b. At two, four and more than four weeks of treatment 4(7%), 2(4%) and one patient (2%) showed jaundice. One patient presented cytolysis during therapy. Regarding anemia, 12(24%) patients had anemia at 2 weeks, 14(28%) at 4 weeks and 10(20%) at more than 4 weeks after baseline. Subjective complaints included: headache 10(20%) cases, nausea 7(14%) cases, fatigue 7(14%) cases, pruritus 2(4%) cases and 1(2%) case each of: gingival bleeding, depression, insomnia, dry mouth, edema and weight loss. Ribavirin dose reduction was needed in 4(8%) patients. None of the patients stopped the treatment due to side effects. All 50 patients had EOT response.

**Conclusion:** The most common side effect among patients in the study group was anemia (24%), while the most frequent subjective complain was headache (20%). None of the patients had to stop the treatment due to side effects. All 50 patients had EOT response.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1138 DISTURBANCES OF VITAMIN D–PARATHYROID HORMONE AXIS IN HEPATITIS C VIRUS INFECTED PATIENTS

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**Introduction:** 25-hydroxyvitamin D (25[OH]D) is produced in the liver from vitamin D. Studies correlating 25(OH) D-PTH status and severity of the various chronic liver injuries reported conflicting results.

**Aims & Methods:** Our aim was to determine the prevalence and type of vitamin D–parathyroid hormone (PTH) disturbance in a homogeneous cohort of ambulatory patients with non-cirrhotic chronic hepatitis C (CHC) and its relationship with disease severity and liver function in northern Taiwan (latitude, 25° 2' 21'' N). We studied 66 consecutive outpatients (28 men, 38 women; mean age, 52.7 ± 13.7 [SD] y) with non-cirrhotic CHC. Serum concentrations of 25(OH) D, PTH, calcium, phosphate, magnesium, creatinine, and liver function tests were determined.

**Results:** Serum 25(OH) D levels were inadequate in 25 patients: vitamin D deficiency (10 ng/mL) was found in 3 patients and vitamin D insufficiency (11–20 ng/mL) was found in 22 patients. Fifteen (22.7%) patients had PTH levels lower than the lower level of reference interval (10 pg/ml). The severity of chronic hepatitis C according to HALT-C formula showed insignificant correlation with the serum 25(OH) D concentration (Table 1). The mean serum concentration of 25(OH) D was similar in 3 groups (P = 0.466). Nine of group 3 patients had a desirable level of serum 25(OH) D. The percentages of subjects with hypovitaminosis D ( 20 ng/mL) were as follows: group 1, 58.8%; group 2, 30.6%; and in group 3, 30.8%. There was no significant correlation between vitamin D and serum level of PTH, calcium, phosphate, ALT, AST,

ALP, urea, creatinine, platelet count, hemoglobin, serum albumin, INR or serum bilirubin.
**Conclusion:** Vitamin D inadequacy exists in CHC patients without cirrhosis but does not correlate with the severity of the disease. In addition, low PTH levels occur in CHC but the explanation is still ill-defined. Therefore, we recommend that future trial should evaluate the economic efficacy of vitamin D supplementation in CHC and the impact of low PTH levels on virologic response rates during and after treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1139 SHEAR WAVE ELASTOGRAPHY OF THE LIVER AND SPLEEN IN PATIENTS WITH AUTOIMMUNE HEPATITIS AND ITS VARIANTS – A SINGLE CENTRE STUDY


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**Introduction:** Autoimmune hepatitis (AIH) is a chronic liver disease which may lead to advanced fibrosis and cirrhosis. Unlike in viral etiology, data on elastographic assessment of liver fibrosis in AIH is scant and virtually do not exists in terms of spleen elastography.
**Aims & Methods:** The aim of this study is to evaluate the potential association between shear wave elastography (SWE) of the liver and spleen with various parameters including serum fibrosis markers in patients with autoimmune hepatitis (AIH) and AIH variants. Fifty consecutive in and out-patients (M/F (16/34, mean age: 37 yrs.) with AIH and its PSC and PBC variants defined according to recent EASL Clinical Practice Guidelines (J Hepatol 2015) were included. They underwent liver and spleen SWE (SuperSonic Imagine Aixplorer®). Different biochemical tests were performed including fibrosis markers and non-invasive tests: Fibrosis-4, aspartate aminotransferase (AST)-to-platelet ratio index (APRI), AST-to-alanine aminotransferase (ALT) ratio (AAR), APRI, FibroQ and Model For End-Stage Liver Disease (MELD) score. Pearson correlation coefficients analysis with was performed and p values $<0.05$ were considered significant.
**Results:** 13 patients (26%) fulfilled elastographic criteria for diagnosing liver cirrhosis. Liver SWE showed a significant correlation with spleen SWE ($p < .05$), AST ($p < .001$), ALT ($p < .01$), alkaline phosphatase (ALP)($p < .001$), INR ($p < .001$) and MELD ($p < .001$), Fibrosis-4 ($p < .001$), APRI ($p < .001$) and Fibro-Q ($p < .05$). There was also a significant, negative correlation between Liver SWE and platelet count ($p < .01$) and serum albumin ($p < .001$). Of interest, spleen SWE correlated with Fibrosis-4 ($p < .05$) and showed a negative correlation with platelet and serum albumin ($p < .05$).
**Conclusion:** Liver SWE could be of use in a non-invasive assessment of liver fibrosis in patients with AIH and its variants. The possible role of spleen SWE in the assessment of portal hypertension in AIH has to be established in larger cohorts of patients however, present results may suggest that it can potentially serve as an additional modality in evaluation of patients suffering from liver autoimmune diseases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1140 IS THERE ANY PROGNOSTIC IMPACT OF EXTRA-HEPATIC SYSTEMIC CONDITIONS IN PRIMARY BILIARY CHOLANGITIS?


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**Introduction:** Primary Biliary Cholangitis (PBC) can be associated with extrahepatic conditions (EHC). These conditions can negatively influence the clinical course of disease. The prognostic implication of EHC is not well established.
**Aims & Methods:** Aims: To determine the prevalence, predictors and prognosis of EHC in PBC. Methods: Case-control retrospective study of PBC patients between 2000–2014. Patients with PBC and EHC (cases) were compared with patients with PBC without EHC (controls). Variables evaluated included age, gender, clinic, biochemical profile, histology, autoimmune profile, Child-Turcotte-Pugh, MELD and Mayo-Risk scores, and prognostic variables, including extrahepatic tumors development, necessity of liver transplantation and overall mortality or PBC-related mortality.
**Results:** Of a total of 82 patients with PBC, 53.7% ($n = 44$) had more than one extrahepatic manifestations, mostly with combination of different conditions (56.8%;25/44). Systemic manifestations preceded the PBC diagnosis in 34.1% (15/44), with an average pre-diagnostic time of $7.6 \pm 7.5$years. The most frequent EHC were rheumatologic (93.2%;41/44), mainly osteoporosis (50.0%;11/53), Sjögren Syndrome (26.8%;11/41) and Scleroderma (17.1%;7/41). After multivariable analysis, the risk factors associated with EHC occurrence were > 7years of PBC, (cut-off 7: AUROC 68.7%; OR 2.700;$p = 0.040$), hypertensive gastropathy (OR 7.299;$p = 0.020$), serum LDH at diagnosis > 203U/L (cut-off 103: AUROC 72.9%; OR 5.313;$p = 0.006$) and serum rheumatoid factor positivity (OR 7.425;$p = 0.020$). Patients with EHC had worse prognosis: cirrhosis complications, need of liver transplantation with overall mortality (63.6%vs36.8%;$p = 0.015$) or with PBC-related mortality (61.4%vs36.8%;$p = 0.027$). However, no differences in survival curves for overall mortality (Kaplan-Meier curve:log-rank-test 0.371;$p = 0.542$) and PBC-related mortality (Kaplan-Meier curve:log-rank-test 0.557;$p = 0.455$) or extrahepatic tumors frequency (20.5%vs7.9%;$p = 0.109$).
**Conclusion:** EHC are frequent and multiple, preceding PBC diagnosis in 1/3 of cases. They are associated with poor prognosis, including cirrhosis complications, need of liver transplantation, overall mortality and PBC-related mortality, despite of no impact in patients' survival curves.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1141 EFFECT OF FIBRATE-ADD-ON TREATMENT IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH AN INSUFFICIENT RESPONSE TO URSODEOXYCHOLIC ACID (UDCA)


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**Introduction:** Ursodeoxycholic acid (UDCA) is the treatment of choice for patients with primary biliary cholangitis (PBC), although a substantial proportion of patients do not respond fully to UDCA treatment. In this respect, fibrates – acting via peroxisome proliferator-activated receptors (PPARs) - have been shown to exert additional beneficial effects on cholestatic liver enzymes and ameliorate pruritus.
**Aims & Methods:** Aim of this study was to investigate the effect of fibrate add-on treatment in patients with an insufficient biochemical response to UDCA.
**Patients:** 22 PBC patients (female: 17[xx%], age: $57 \pm 11$years [mean $\pm$ SD], BMI $25 \pm 3.4\,kg/m^2$, duration of treatment with UDCA $9 \pm 6$years) treated with bezafibrate 400 mg/d for at least 6 months in addition to UDCA after an incomplete biochemical response (Alkaline phosphatase (AP) > ULN) to UDCA (13–15 mg/kg/d) were included. AP, Gamma-glutamyl transpeptidase (GGT), serum creatinine, triglycerides (TG) and serum cholesterol were analyzed at baseline and during treatment every 3 months.
**Results:** AP and GGT decreased during bezafibrate add-on treatment (APbaseline $190.6 \pm 84$, AP3months $119.4 \pm 66.7$, AP9months $112 \pm 69.5$ U/L, mean $\pm$ SD, $p \leq 0.01$ when compared to baseline). 15/68% of patients reached AP levels within the normal range. We did not observe any effect on serum creatinine in our patients treated with UDCA and bezafibrate (Creabaseline $0.77 + 0.24$, Crea3months $0.78 + 0.36$, Crea9months $0.75 + 0.41$ mg/dl). Serum cholesterol and TG did not change (table 1).
**Conclusion:** Fibrate treatment is an effective adjunct therapy for patients with PBC and an insufficient response to UDCA. Within our treatment period we did not observe worsening of renal function. No adverse events were reported.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Table 1.**

| | Baseline | 3 Months | 9 Months |
|---|---|---|---|
| AP (U/L) | $190.6 \pm 84$ | $119 \pm 66.7$* | $112.3 \pm 69.5$* |
| GGT (U/L) | $166.3 \pm 145$ | $116.4 \pm 129.5$* | $136.6 \pm 109$* |
| Serum Creatinine (mg/dl) | $0.77 \pm 0.24$ | $0.78 \pm 0.36$ | $0.75 \pm 0.41$ |
| Triglycerides (mg/dl) | $119 \pm 56$ | $89 \pm 46$ | $100 \pm 56$ |
| Serum Cholesterol (mg/dl) | $202.2 \pm 56.3$ | $198.2 \pm 78.3$ | $199 \pm 104$ |

AP, GGT, Serum Creatinine, TG and Serum Cholesterol during treatment with bezafibrate (mean$\pm$SD, *$p < 0.01$ [when compared to baseline in a paired T-Test])

### P1142 SERONEGATIVE PRIMARY BILIARY CHOLANGITIS: A DISTINCT ENTITY?


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**Introduction:** Anti-mitochondrial antibody (AMA) is a diagnostic marker in Primary Biliary Cholangitis (PBC), because of the high sensitivity and specificity. However, 5–10% of patients with clinical, biochemistry and histology consistent

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| Elastography technique | Fasting^ (KPa) | 30 minutes after food intake** (KPa) | 1 hour after food intake*** (KPa) | 2 hours after food intake**** (KPa) | |
|---|---|---|---|---|---|
| **2D-SWE** | 5.73 ± 1.18 | 5.64 ± 1.07 | 5.56 ± 0.96 | 5.61 ± 0.95 | p^** = 0.69 p^*** = 0.43 p^**** = 0.57 |
| **2D-SWE.GE** | 5.24 ± 0.23 | 5.47 ± 0.16 | 5.2 ± 0.23 | 5.20 ± 0.24 | p^** = 0.42 p^*** = 0.90 p^**** = 0.91 |

with PBC are seronegative. The characterization and clinical significance of this subgroup of patients remain unclear.
**Aims & Methods:** Aims: Determine at the diagnosis, the clinical, biochemical, serological and histological profiles and the prognosis of patients with seronegative PBC. Methods: Case-control retrospective study of inpatients in gastroenterology unit, between 2000–2013, with seronegative PBC diagnosis (cases) and positive AMA (controls). Variables evaluated included clinical, biochemical, autoimmune profile and pathology, as well as prognosis, including portal hypertension complications, mortality or liver transplantation necessity.
**Results:** Of the total of 93 patients with PBC, 13(14.0%) were seronegative. In cases group, there was a significantly lower proportion of women (69.2%vs78.8%;p = 0.001), but similar age of diagnosis (54±18vs54±14yo;p = 0.071) and follow-up of the disease (9±5vs8±5yo;p = 0.818). Relatively to the clinic, the most cases were symptomatic (92.3%vs72.5%;p = 0.049), mainly jaundice (53.8%vs7.9%;p = 0.001), fatigue (69.2%vs42.5%;p = 0.256), pruritus (53.8%vs36.2%;p = 0.577) and portal hypertension complications (15.4%vs8.8%;p = 0.508). Dyslipidemia was more frequent in cases (61.5% vs48 .8%;p = 0.026), but there were no significant statistically differences in the biochemical and immunological profiles. In respect to serological/autoimmunity characterization, cases presented more positivity to ANA (76.9%vs55.4%;p < 0.001), SML (15.4%vs1.2%;p < 0.001), anti-SSA (7.7%vs0.0%;p < 0.001) and anti-parietal cells (46.2%vs38.0%;p < 0.001), and more frequency of other autoimmune diseases (69.2%vs23.8%;p = 0.001): Raynaud's phenomenon (23.1%vs5.0%;p = 0.049), diabetes mellitus type 1 (23.1%vs2.5%;p = 0.008), autoimmune hepatitis (23.1%vs1.25%;p = 0.001) and idiopathic thrombocytopenic purpura (7.7%vs0.0%;p = 0.043). At histological level, there were a cases predominance of stage I (44.4%vs30.8%;p = 0.451), stage IV (33.3%vs21.5%;p = 0.462), severe hepatocellular and piecemeal lymphocytic necrosis (25.0%vs1.7%;p = 0.007) and lobular necrosis (25.4%vs1.7%;p = 0.013). There were no significant statistically differences in the Mayo risk score, mortality, death causes and need/time of disease to liver transplantation.
**Conclusion:** At the diagnosis, patients with seronegative PBC have more symptoms, dyslipidemia, other autoimmune diseases and hepatocellular necrosis in the histology. However, there was no prognostic implications relatively to portal hypertension complications, mortality or liver transplantation necessity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1143 CARDIOVASCULAR RISK ASSESSMENT IN PRIMARY BILIARY CHOLANGITIS: A SYSTEMIC DISEASE?

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**Introduction:** Like other cholestatic liver diseases, there is hypercholesterolemia in primary biliary cholangitis (PBC), due to the supression of bile acids secretion, mainly in advanced stage. Despite frequent, the dyslipidemia impact at cardiovascular level remains unclear.
**Aims & Methods:** Aims: Determine the frequency of dyslipidemia before ursodesoxycholic acid tretment in PBC and its impact on cardiovascular risk (nonfatal/fatal heart and cerebrovascular events, clinically relevant). Methods: Case-control retrospective study of inpatients in gastroenterology unit, between 2000–2013, with PBC diagnosis (G1-cases:93 patients) and diverticular colic disease (DCD) without autoimmune diseases (G2-controls:101 patients), and between PBC without cardiovascular risk factors (G3-cases:22 patients) and DCD without cardiovascular risk factors (G4-controls:23 patients).
**Results:** PBC patients were mostly middle-aged women (women:75vs56, p < 0.001; age: 54 ± 15vs73 ± 14yo, p < 0.001). Dyslipidemia was more frequent in cases (51.6%vs19.8%, p < 0.001), with total-cholesterol 223 ± 76, LDL-cholesterol 115.8 ± 83.8, HDL-cholesterol 50 ± 18 and triglycerides 141 ± 102; however hypertension (38.7%vs60.4%;p = 0.003) and mellitus diabetes (16.1%vs28.7%;p = 0.027) were more frequent in the controls. Vascular events occurred in 22.6% of patients (vs24.8%;p = 0.722), 11.8% of witch was cardiovascular events (vs20.8%;p = 0.093): 5-acute myocardial infarction; 6-ischaemic heart disease; and 15.0% cerebrovascular events (vs5.9%;p = 0.037): 7-transient ischemic accident; 6-ischemic stroke; 1-hemorrhagic stroke. Of cases, 11.8% died due to no cardiovascular cause. Relatively to Mayo risk score at the diagnosis, the majority of cases presented low risk (54.8%), with more dyslipidemia (60.8%vs40.5%;p = 0.043) and cardio/cerebrovascular events (27.4%vs16.7%;p = 0.174), compared to intermediate/high risk. In relation to the histological stage at the diagnosis, there were more cases in stage I (31.1%) and stage II (31.1%), with more dyslipidemia (stageI:52.2%;stageII:56.5%) and cardio/cerebrovascular events (stageI:39.1%;stageII:17.4%). After cardiovascular risk factors exclusion (G3vsG4), there was no significant statistically difference in the frequency of cardiovascular (4.5%vs21.7%;p = 0.090) and cerebrovascular events (4.5%vs4.3%;p = 0.974).
**Conclusion:** PBC patients have more dyslipidemia, however without more nonfatal/fatal cardiovascular risk compared to the patients without PBC. Therefore, preventive strategies of vascular events should be the same of those for the general population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1144 THE INFLUENCE OF FOOD INTAKE ON LIVER STIFFNESS MEASUREMENTS OBTAINED BY TWO 2D-SWE METHODS

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**Introduction:** The liver stiffness measurements obtained by ultrasound based elastographic methods may be influenced by different factors.
**Aim**: The aim of the study was to assess the influence of food intake on liver stiffness values obtained by two 2D-SWE techniques 2D-SWE and 2D-SWE.GE.
**Material and Methods:** 2 groups of healthy volunteers in whom liver stiffness measurements were performed first in fasting condition, followed by measurements made at 30 minutes, 1 h, 2 h after food intake, were included in this study. All subjects received the same standard solid meal. **Group 1** included 50 subjects (39 female, 11 male) in whom the liver stiffness was assess by 2D Shear Waves Elastography-[Aixplorer, Supersonic Imagining (SSI) ], valid measurements being defined as the median value of 3 measurements acquired in a homogenous area. **Group 2** included 33 subjects (20 female, 13 male) in whom the liver stiffness was assess by 2D-SWE.GE-(LOGIC E9, General Electric), valid measurements being defined as the median value of 10 measurements. For both groups the mean values of liver stiffness on fasting, at 30 minutes, 1 h, 2 h after food intake were calculated and compared.
**Results:** The liver stiffness values did not increase after food intake neither for 2D-SWE, nor for 2D-SWE.GE (table). Table. Liver stiffness values on fasting and after food intake.
**Conclusion:** Our preliminary results show the food intake did not significantly increased the LS values obtained by 2D share wave elastography techniques.
**Disclosure of Interest:** I. Sporea: Speakers' Honoraria or Congress Participation support or Consultant/Advisory Board Fee from the following companies: Philips, Siemens, General Electric, Abbvie, MSD, BMS, Astra Zeneca, Berlin Chemie Menarini
All other authors have declared no conflicts of interest.

## P1145 CORRELATION OF LIVER STIFFNESS MEASUREMENT ON TRANSIENT ELASTOGRAPHY WITH INCIDENCE OF HYPOVASCULAR HYPOINTENSE NODULE ON GADOXETIC ACID-ENHANCED MRI IN PATIENTS WITH HEPATITIS B VIRUS

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**Introduction:** There have been some reports which evaluated the imaging features of hypovascular hypointense nodules on gadoxetic acid-enhanced MR images in patients with chronic liver disease that may be related with progression to hypervascular HCC. However, to the best of our knowledge, there has been no report which evaluated relationship between hypovascular hypointense nodule and many baseline characteristics including liver cirrhosis. The purpose of this study was to evaluate the correlation of liver stiffness measurement based on transient elastography with hypovascular hypointense nodule on gadoxetic acid-enhanced magnetic resonance imaging (MRI) in patients with hepatitis B virus (HBV).
**Aims & Methods:** This retrospective study was approved by the institutional review board, and the requirement for informed consent was waived. Between August 2012 and March 2016, consecutive 430 patients with HBV who had received transient elastography for liver stiffness measurement and gadoxetic acid-enhanced MRI were retrospectively analyzed. The patients were divided into two groups according to the presence or absence of hypovascular hypointense nodule. Baseline characterisctis including presence of liver cirrhosis, hepatocellular carcinoma, viral hepatitis, alcoholic liver disease and level of biologic markers were compared between the two groups. The correlations between incidence of hypovascular hypointense nodule on gadoxetic acid-enhanced MRI and the degree of fibrosis stage F0 from F4 on the METAVIR scale were assessed using linear-by-linear association.
**Results:** Except presence of liver cirrhosis, there was no significant difference in baseline characteristics including coexisting with hepatocellular carcinoma in both groups. Median liver stiffness values measured using transient elastography was 11.8 (range, 3–75). The degrees of fibrosis stage in patients included were 46 in F0, 60 in F1, 65 in F2, 35 in F3, and 224 in F4, respectively. The

incidence of hypovascular hypointense nodule on gadoxetic acid-enhanced MRI tended to be increase with the degree of fibrosis stage ($p = 0.047$).
**Conclusion:** The incidence of hypovascular hypointense nodule on gadoxetic acid-enhanced MRI Liver in patients with HBV was associated with the degree of liver fibrosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1146 THE PERFORMANCE OF 2D-SWE.GE COMPARED TO TRANSIENT ELASTOGRAPHY FOR THE EVALUATION OF LIVER STIFFNESS


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**Introduction:** Chronic liver diseases encountered in daily practice are due to chronic viral infections or to other conditions, such as alcoholic steato-hepatitis (ASH) or non-alcoholic fatty liver disease (NAFLD). The evaluation of chronic liver disease's severity is mandatory, for a decision regarding therapy or to establish prognosis. For many years, liver biopsy (LB) was the only method to evaluate such patients and it is still considered the "gold-standard" method. In the last years non-invasive modalities for liver diseases' assessment are being used more and more in daily practice, especially in Europe.
**Aims & Methods:** The current study's aim is to evaluate the performance of 2D-SWE.GE in noninvasive fibrosis assessment as compared to a validated method-Transient Elastography (TE) and to identify liver stiffness (LS) cut-off values for predicting different stages of liver fibrosis, considering Transient Elastography (TE) as the reference method, since it is a validated method for liver fibrosis assessment (EASL Guidelines). Our prospective study included 307 consecutive subjects with or without chronic hepatophaties (only compensated liver disease evaluated for decision regarding treatment), in which liver stiffness (LS) was evaluated in the same session by means of 2 elastographic methods: TE (M or XL probes) and 2D-SWE.GE (LOGIQ E9, GE Healthcare, Chalfont St Giles – UK). Reliable LS measurements were defined as follows: for TE – the median value of 10 measurements with a success rate of $\geq$60% and an interquartile range $<$ 30% and for 2D-SWE.GE - the median value of 10 measurements acquired in a homogenous area and an interquartile range (IQR) $<$ 30%. To discriminate between various stages of liver fibrosis by TE we used the following cut-offs (kPa): F1–6; F2- 7.2; F3- 9.6; F4- 14.5.[1]
**Results:** Reliable LS measurements were obtained in 292/307 (95.1%) subjects by 2D-SWE.GE, and in 291/255 (94.7%) by TE ($p = 0.975$). The final analysis was performed on 278 subjects with valid measurements by both methods. Based on TE cut-off values we divided our cohort into the following groups: F $<$ 2: 79/278 (28.4%); F = 2: 13/278 (4.7%); F = 3: 44/278 (15.9%) F = 4: 142/229 (51%). We found a strong correlation between the LS values obtained by the 2 methods: $r = 0.825$, $p < 0.0001$. The mean values obtained by 2D-SWE.GE considering TE cut-off values as reference were: F $<$ 2: **5.76** $\pm$ 1.51 kPa; F = 2**: 7.24** $\pm$ 1.7 kPa; F = 3: **10.47** $\pm$ 1.89 kPa; F = 4: **13.55** $\pm$ 2.76 kPa ($p < 0.001$). The best cut-off value for F $>$ 2 was **6.7** kPa (AUROC = 0.967, Sensitivity = 95.96%, Specificity = 85%), for F $>$ 3 was **8.6** kPa (AUROC = 0.977, Sensitivity = 94.05%, Specificity = 90.32%) and for F $>$ 4 was **10.7** kPa (AUROC = 0.934, Sensitivity = 87.32%, Specificity = 86.03%).
**Conclusion:** 2D-SWE.GE and TE had good feasibility (95.1% and 94.7%) with no statistical differences between them ($p = 0.975$). There was a strong correlation between the two methods, with LS values significantly increasing with the severity of fibrosis. The best 2D-SWE.GE cut-off values for predicting F $>$ 2, F $>$ 3 and F $>$ 4 were 6.7 kPa, 8.6 kPa and 10.7 kPa.
**Disclosure of Interest:** I. Sporea: Ioan Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric.
R.L.D. Sirli: Roxana Sirli received speaker fees from Philips
A. Popescu: Alina Popescu received speaker fees from Philips
All other authors have declared no conflicts of interest.

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### P1147 INFLUENCING FACTORS ASSOCIATED WITH DIAGNOSTIC ACCURACY OF REAL-TIME SHEAR WAVE ELASTOGRAPHY IN CHRONIC HEPATITIS B PATIENTS WITH LIVER FIBROSIS


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**Introduction:** Real-time shear-wave elastography, as a novel stiffness measurement method of hepatic fibrosis, allows quantitative detection of larger liver specimens in real time with two-dimensional shear wave generating from tissue directly, which overcome the shortcomings of Transient elastography and Point shear wave elastography to some extent. However, whether the advantages of SWE can decrease interruption of factors identified in other elastography remains unclear.
**Aims:** To identify factors influencing the performance of SWE and investigate their effect.
**Methods:** Patients with chronic hepatitis B (CHB) were included from July 2013 to February 2016 at the First Affiliated Hospital of Sun Yat-sen University were included. Fibrosis stage were acquired according to liver biopsy or clinically diagnosed decompensated cirrhosis Liver stiffness were assessed with SWE (Supersonic Imagine, France) and parameters of anthropometry, liver inflammation score, hepatic enzymes levels, virology (HBV DNA levels, HBsAg titre) and metabolism (lipid profile, glucose, insulin, and uric acid concentrations) markers were measureed. Logistic regression model was performed to identify factors that correlated with discordance between historic results and SWE. Effect of factors was assessed by comparing the Receiver operating characteristic curve (ROC) between patients with or without these factors.
**Results:** The analysis was included in 261 CHB patients (133 undergone liver biopsy and 128 decompensated cirrhosis). 192 (73.6%) patients were males and the average age was 38.6(16~54) years. ①The Area Under ROC (AUC) for liver stiffness measurement with SWE were 0.861, 0.932 and 0.910 for the diagnosis of significant fibrosis (7.8kpa, $\geq$ F2), advanced fibrosis (8.9 kpa, $\geq$F3) and cirrhosis (9.4kpa, F4), respectively. ② When predicting the liver fibrosis stage with cut-off values of SWE, overall misdiagnostic rate was 6.51%, omission diagnostic rate was 11.9%. ③The risk of discordance between SWE and historical results with multivariate analysis was associated with ultrasonic sign of fatty liver ($P = 0.048$, OR = 2.23.95%CI:1.01–4.94), liver inflammation activity score over 1 ($P = 0.01$, OR = 2.12.95%CI:1.20–3.73) and fibrosis stage ($P = 0.046$, OR = 0.74.95%CI:0.54–0.96).Liver inflammation activity score over 1 also ($P = 0.037$, OR = 2.10.95%CI:1.05–4.22) predicted overestimation of SWE while no variables were considered to predict of underestimation for the assessment of fibrosis. ④AUC of CHB patienrs with liver inflammation activity score over 1 was inferior to those without when SWE was applied to distinguish significant fibrosis (0.756 vs 0.891, $p = 0.021$) instead of other stage, as well as the AUC of patients with ultrasonic sign of fatty liver to those without (0.703 vs 0.938, $p = 0.000$)
**Conclusion:** SWE can differentiate liver fibrosis accurately. The presence of inflammation of pathology and ultrasonic sign of fatty liver is the main factor that decrease the accuracy of SWE.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1148 TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT – EIGHT YEARS OF EXPERIENCE OF A PORTUGUESE CENTER


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**Introduction:** The purpose of transjugular intrahepatic portosystemic shunt (TIPS) is to decompress portal venous system and prevent rebleeding from varices in patients who fail pharmacologic and endoscopic treatment, or reduce the formation of diuretic refractory ascitis, among other less common indications. Recent data suggest that achieving a portal pressure gradient below 12 mmHg for variceal bleeding and below 8 mmHg for refractory ascitis is the optimal technical end-point.

**Aims & Methods:** We present the results of TIPS procedures of a Portuguese referral center from October 2007 to December 2015. Data were collected retrospectively from hospital records. Since January 2015, the procedure protocol includes record of the pressure gradient after TIPS. A secondary objective of this study is to compare the outcome of the group of patients that were submitted to TIPS without hemodinamic measurements and the group submitted to TIPS with portal pressure measurements.
**Results:** During the study period, 143 patients were proposed for TIPS. 79% of patients were males and the average age was 54.6 years. Primary liver disease was alcoholic in 67.1%, mixed alcoholic/viral in 14%, viral in 10.5% and other in 9.1%. Indications for TIPS were: refractory ascitis (62.2%), variceal bleeding (34.2%) and hydrothorax (3.5%), MELD and Child-Pugh scores before TIPS were 13.88+-4.95 and 8.62 + -1.6. Pre-existing encephalopathy was recorded in 15.4%. Technical success rate was 92.3% (n = 132). Hemodynamic success rate (since january 2015) was 81.3% for refractory ascitis and 100% for variceal bleeding indications. MELD and Child-Pugh scores 1 and 6 months after TIPS were 17+-7.2, 9.5+-1.6, 16+-5.7 and 8.8+-1.8, respectively. Outcome analysis by indication showed that 40.5% (n = 34) patients with refractory ascitis experienced improvement. Rebleeding rate was 16.3%. One patient presented with de novo variceal GI bleeding. In 3 patients with hydrothorax, records showed improvement in fluid retention, though data was not available for the other two patients. When considering the results before and after routine hemodinamic-guided TIPS dillation, there was no statistical difference in ascitis improvement, rebleeding rate or encephalopathy development. 37.9% with TIPS were transplanted during follow up (284.1+- 243.5 days). Mortality in patients not submitted to liver transplantation was 41.5 (226.1+-257.7 days) 4.2% had immediate, procedure-related complications: haemoperitoneum 1.4%, porto-billiary fistula 0.7%, haemorrhagic shock 0.7%, cervical haematoma 0.7%, anestesia complication 0.7%. Most common clinical complications after TIPS placement were: encephalopathy (newly installed or worsened)–27.3%, TIPS thrombosis in 8.3%, hiperdynamic circulation or cardiac failure–5.3%, TIPS infection 0.8%, haemolytic anaemia 0.8%, worsening of acute liver failure 0.8%, pulmonary thromboembolism 0.8%, other not specified-3.8%.
**Conclusion:** This is an evolving experience in a Portuguese referral center. When analysing this results, it is important to bear in mind that techinical practices have changed over the last decade, with introduction of covered stents that are less prone to thrombosis or other complications. Outcomes on ascitis should be assesed with caution, since data on diuretic therapy adjustment were lacking. It is possible that some partial responders were not included due to lack of records. Rebleeding rate was higher than expected. However, data on timing of rebleeding was lacking, as was the endoscopic site. Hence, we can not exclude bleeding from previous elastic band scarring, a complication of endoscopic treatment, not a failure of TIPS. In recent years, our protocol of TIPS for variceal bleeding also includes endovenous cyanoacrylate obliteration of upper GI varices, therefore we expect the rate of recurrence of GI bleeding to drop in the following years. Our data did not show improvement in outcome with hemodinamic-guided TIPS dillation at placement, although the number of patients in the second group is small (n = 22) which could bias the results. Although not exsempt of complications, TIPS remains an important salvage technique in difficult to treat patients with portal hypertension.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1149 SERPINB3 MAY AFFECT LIVER CANCER PROGRESSION BY DIFFERENTLY REGULATING HYPOXIA INDUCIBLE FACTORS - 1A AND -2A

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**Introduction:** SerpinB3 is a hypoxia and hypoxia-inducible factor (HIF)-2$\alpha$ up-regulated cysteine-proteases inhibitor overexpressed in hepatocellular carcinoma (HCC). SerpinB3 has been reported to act as a paracrine mediator able to up-regulate, in normoxic conditions, HIF1$\alpha$ and HIF2$\alpha$ as well as their related target genes in liver cancer cells, with differential regulation of their expression and stabilization. The ubiquitin-like molecule NEDD8 is a key regulator of cell growth, viability and malignant transformation and neddylation promotes stabilization of proteins with essential regulatory roles. Overexpression of global neddylation has been detected in HCC and suggested to be associated with its poorest prognosis.
**Aims & Methods:** The present study has been designed to investigate the mechanisms by which SerpinB3 can induce up-regulation of HIF1$\alpha$ and HIF2$\alpha$ in liver cancer cells. The cross-talk between S-B3 and HIF1$\alpha$/HIF2$\alpha$ has been investigated by taking advantage of morphological, molecular, biochemical and cell biology techniques in the following experimental models: i) control HepG2 stably transfected with empty vector; ii) HepG2 stably transfected to overexpress SerpinB3 (HepG2/SB3); iii) transgenic mice overexpressing SerpinB3 in the liver.
**Results:** Immunohistochemistry performed on liver sections from SerpinB3 transgenic mice shows immune-positivity for HIF1$\alpha$ and HIF2$\alpha$ not only around centrilobular vein, but also in hepatocytes of the entire parenchyma, with a more impressive level of nuclear staining for HIF2$\alpha$ vs HIF1$\alpha$. Different experimental approaches revealed that SerpinB3, in normoxic conditions, differentially regulate HIF1$\alpha$ and HIF2$\alpha$ up-regulation: i) SerpinB3 increases transcription of HIF1$\alpha$, but not HIF2$\alpha$; ii) the up-regulation of HIF1$\alpha$ protein levels is rapid and transient and results in up-regulation of target genes involved in anaerobic glycolysis; iii) Seahorse metabolic analysis revealed an increase of ECAR (ExtraCellular Acidification Rate) and a reduction of OCR (Oxygen Consumption Rate) parameters; iv) increased HIF2$\alpha$ protein levels and related target genes are dependent on its selective neddylation/stabilization but not on an inhibition of overall proteasome activity by SerpinB3; v) the use of a specific siRNA of NAE-1 (NEDD8 Activating Enzyme-1) selectively reduces HIF2$\alpha$, but not HIF1$\alpha$, protein levels.
**Conclusion:** SerpinB3 can affect the behaviour of target cells by increasing protein levels of HIF1$\alpha$ and HIF2$\alpha$, with HIF1$\alpha$ that facilitates cell survival in harsh microenvironment by inducing early cellular metabolic switch to glycolytic phenotype. On the other hand neddylation/stabilization and nuclear translocation of HIF2$\alpha$ promotes proliferation and tumor progression.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1150 P53 TRANSCRIPTION FACTORS CONTROL APOPTOSIS SUSCEPTIBILITY BY REGULATION OF MCL1

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**Introduction:** Hepatocellular carcinoma (HCC) represents a complication of liver cirrhosis limiting the curing option by liver transplantation. Depending on their splice variants – with transactivation (TA) domain or dominant negative (DN) - p53-family transcription factors (p53, p63, p73) exert tumorsuppressive or oncogenic functions in cell cycle by transcriptional regulation of a specific set of genes. In previous studies we identified the MCL1 gene (Myeloid cell leukemia sequence 1, Mcl-1) as potential target gene of the p53 family and confirmed its prognostic relevance in HCC. Mcl-1 is a member of the Bcl-2 protein family being involved in the control of mitochondrial integrity. Mcl-1 represents an anti-apoptotic member of the Bcl-2 family, supporting cell survival by binding and inhibition of pro-apoptotic Bcl-2 proteins.
**Aims & Methods:** Aim of this study was to elucidate the impact of p53 family members on MCL1 gene regulation. Hep3B cells were transfected with rAd-GFP, -p53, -TAp63$\alpha$, -TAp73$\beta$, -DNp63$\alpha$, and DNp73$\beta$. MCL1 expression was measured by real time qPCR. Western Blot analyses determined intracellular levels of Mcl-1 after specific siRNA interference. Potential binding sites of p53 family members in the MCL1 locus were identified by database analyses (pDraw32, Husar, MatchTM) and verified by luciferase reporter assays. Direct protein interactions of Mcl-1 and p53 proteins were evaluated by LUminescence-based Mammalian IntERactome mapping (LUMIER) technology.
**Results:** p53 and the isoforms TAp63 and TAp73 inhibited MCL1 expression, whereas $\Delta$Np63$\alpha$ and $\Delta$Np73$\beta$ induced transcription of the MCL1 gene. These effects were confirmed for Mcl-1 protein levels. Reduction of Mcl-1 protein levels was abrogated after silencing of p53, TAp63 and TAp73. Database analyses identified two potential p53 binding sites and one potential p63 binding site each in promoter, intron 1 and 2 of the MCL1 gene. Luciferase reporter assays of these cloned putative binding sites confirmed a regulation of the MCL1 gene by p53 family members. Furthermore, a direct protein-protein interaction of Mcl-1 with p53 and TAp63, respectively, was detected.
**Conclusion:** p53 family members directly regulate the expression of the MCL1 gene. p53, TAp63 and TAp73 are potent repressors, whereas DNp63 and DNp73 act as inducers of MCL1. On posttranslational level, Mcl-1 interacts with p53 and TAp63. Since Mcl-1 has anti-apoptotic functions, a downregulation of Mcl-1 by TA-isoforms of p53 proteins results in an increase of apoptosis susceptibility. HCC is often associated with chemotherapeutic resistance, which could be overcome by reconstitution with p53, TAp63 and TAp73 or a direct inhibition of Mcl1.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1151 BRG1 PROMOTES HEPATOCARCINOGENESIS BY MODULATING CYCLINB1, D1, E1 AND MATRIX METALLOPROTEINASE 7

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**Introduction:** The chromatin remodeler complex SWI/SNF plays an important role in physiological and pathological processes. The role of BRG1, a catalytic subunit of the SWI/SNF complex, that is known to be mutated in hepatocellular carcinoma (HCC) remains unclear.
**Aims & Methods:** The aim of this work is to investigate the role of BRG1 on cell growth and its effect on the expression of target genes. We examined the expression of BRG1 in human tissue samples and in HCC cell lines by qRT-PCR and Western Blot. In addition, we used siRNA to down-regulate BRG1 in

human HCC cell lines and analysed its effect. Cell growth of siRNA-treated cells was analyzed and the expression of target genes after BRG1 downregulation was investigated in detail.
**Results:** BRG1 was found to be significantly increased in HCC samples compared to non-HCC samples. After BRG1 downregulation by siRNA, cell growth decreased in HuH7 and HepG2 cell lines. A modulating effect of BRG1 could be shown for the expression of CyclinB1, D1, E1, p21, Cdkn2a, Cdkn1b and MMP7 in either HepG2 or HuH7 cell lines. These target genes showed a positive correlation with BRG1 expression.
**Conclusion:** Our results support the hypothesis that overexpression of BRG1 increases cell growth in HCC. Furthermore, the data obtained by qRT-PCR highlight particular genes that are being regulated by BRG1 during hepatocarcinogenesis. In particular, CyclinB1, D1, E1 and MMP7 appear to play a major role in this context and might be an important link between BRG1 expression and HCC development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1152 PROTEIN KINASE CK2 REGULATES ONCOGENIC PROPERTIES OF CHOLANGIOCARCINOMA CELLS

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**Introduction:** Cholangiocarcinoma (CCA) is a malignant tumour arising from cholangiocytes in the biliary tree, characterized by a poor prognosis and alterations in various signaling cascades and genetic mutations (1,2). The mechanisms underlying the CCA occurence and progression are largely unknown. CK2 is a ubiquitous serine-threonine protein kinase (3) which contributes to the malignant phenotype in various types of cancer, and its overexpression is associated with unfavorable prognosis (4,5). CK2 may be targeted by different inhibitors, including CX-4945, that is currently being evaluated in clinical trials (6,7).
**Aims & Methods:** This project aims to understand the role of CK2 in CCA cells, using the selective inhibitor CX-4945 to block its catalytic activity. Human cholangiocarcinoma cells (HuCCT-1 and CCLP1) were cultured by standard methods. CX4945 was used as a specific CK2 inhibitor. CK2 activity was measured using a CK2-specific peptide substrate. Cell cycle progression was analyzed using flow cytometry. Cell migration and cell invasion assays were performed using Boyden chambers.
**Results:** CK2 was found to be highly expressed in the CCA cell lines. Treatment with CX4945 induced a significant reduction of its catalityc activity as measured by kinase assay and phosphorylation levels of a CK2 substrate by western blotting. Pharmacological inhibition of CK2 decreased cell viability, and activated the apoptotic process. Moreover CK2 activity was also found to be necessary for cell cycle progression, as exposure of CCA cells to CX4945 altered cell cycle progression, in particular blocking the G1/S transition. Finally, CK2 inhibition affected the protumorigenic effects of Tgf-$\beta$ in CCA cells, blocking the promotion of epithelial-mesenchymal transition (EMT), cell motility and invasiveness, relevant actions in the progression and metastasis of cholangiocarcinoma.
**Conclusion:** The results obtained in this study indicated that CK2 contributes to the malignant phenotype of CCA cells modulating proliferation, cell cycle regulation and metastatic processes. These data strengthen the need for further investigations in order to characterize the action of CK2 on CCA biology and could contribute in the design and execution of more effective trials with the clinical-grade CK2-inhibitor CX4945 in patients with CCA.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1153 ONCOSTATIN M INDUCES INCREASED INVASIVENESS IN HEPATIC CANCER CELLS THROUGH HIF1A-RELATED RELEASE OF VASCULAR ENDOTHELIAL GROWTH FACTOR A

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**Introduction:** Oncostatin M (OSM), a pleiotropic cytokine that belongs to the interleukin-6 (IL-6) family, has been reported to orchestrate hypoxia-influenced processes such as liver development, liver regeneration and angiogenesis, being then potentially involved in the progression of chronic liver diseases towards cirrhosis and the genesis of hepatocellular carcinoma (HCC). Accordingly, both OSM and its related LIFR$\beta$ (leukemia inhibitory factor receptor $\beta$) receptor subunit were found to be overexpressed in cirrhotic liver. Recently, hypoxia, as an independent signal operating through hypoxia-inducible factors (HIFs), has been shown to induce epithelial-to-mesenchymal transition (EMT) in cancer cells, including HepG2 cells. In this connection, OSM-related signaling pathway has been reported to up-regulate HIF1$\alpha$ and switch on EMT program.
**Aims & Methods:** This study has been designed in order to investigate, in vivo and in vitro, the relationships between OSM, expression of vascular endothelial growth factor A (VEGF-A) and increased invasiveness. EMT, invasiveness, angiogenesis and signal transduction pathways were analyzed by integrating morphological, molecular and cell biology techniques in the following experimental models: i) Liver specimens from HCV cirrhotic patients carrying G1 and G2 HCC; ii) HepG2 and Huh7 cells exposed to human recombinant OSM; iii) HepG2 stably transfected to overexpress OSM or transfected with empty vector.
**Results:** OSM was expressed in HCC in areas also positive for HIFs and VEGF-A, with OSM expression correlating with early recurrence and poor prognosis in HCV cirrhotic patients carrying HCC. Recombinant human OSM induced EMT-related changes within 48–72 hrs and stimulated invasiveness in hepatic cancer cells. Different experimental approaches revealed that OSM-dependent invasiveness is due to release of VEGF and involve activation of PI-3 K, ERK1/2, and p38MAPK: 1) HepG2 cells exposed to human recombinant OSM (hrOSM) lead to an increase of HIF1$\alpha$ and VEGF-A mRNA levels as well as release of VEGF-A protein in culture medium; 2 a) specific pharmacological inhibitors against PI-3 K, ERK1/2, p38MAPK signaling pathways results in decrease of invasiveness induced by conditioned medium collected by HepG2 cells treated with OSM for 48 hrs; 2 b) the same result was obtained using neutralizing antibody raised against Flk-1 (VEGF receptor type 2) or specific inhibitor of Flk-1; 3) HepG2 cells stably transfected in order to overexpress OSM show increased invasiveness and metalloproteinase-2 activity, VEGF-A mRNA levels as well as VEGF-A release in culture medium.
**Conclusion:** OSM, expressed in human HCC, switches on EMT and induces increased invasiveness in human hepatic cancer cells through a mechanism involving HIF1$\alpha$-dependent release of VEGF-A.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1154 METFORMIN AND SORAFENIB SYNERGISTICALLY INDUCE CELL SENESCENCE IN HEPATOCELLULAR CARCINOMA CELLS

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**Introduction:** Sorafenib improves overall survival for patients with advanced hepatocellular carcinoma (HCC); however, the effect is limited. Metformin has been reported to be beneficial in HCC patients' outcome. Whether metformin synergistically interacts with sorafenib to inhibit HCC cells remains unknown.
**Aims & Methods:** The in vitro effect of metformin and sorafenib combination on cell senescence was evaluated on hepG2 and Huh7 hepatoma cell lines. Western blotting was used to detect cyclin-dependent kinase inhibitor p27/Kip1 and cyclin E. Flow cytometry and activation of senescence-associated $\beta$-gal (SA-$\beta$-gal) was used to determine senescence.
**Results:** We found both metformin alone and sorafenib alone therapy led to cell cycle arrest at G0/G1 phase. Combined metformin and sorafenib therapy further increased the effect to inhibit cell cycle arrest. SA-$\beta$-gal activation was found in both metformin alone and sorafenib alone therapy. This senescence effect in HCC cells was significantly higher in combination therapy. In signaling pathway, we found combination therapy synergistically induced Skp2 degradation, which resulted in p27/Kip1 accumulation and cyclin E inactivation.
**Conclusion:** Metformin and sorafenib combination therapy causes HCC cell senescence via the Skp2–p27/Kip1-cyclin E pathway. The clinical significance of our observation needs more studies to confirm.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1155 TARGETING ALDEHYDE DEHYDROGENASE 2: NEW THERAPEUTIC POTENTIAL FOR PREVENTION OF NONALCOHOLIC STEATOHEPATITIS-RELATED LIVER CARCINOGENESIS?

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**Introduction:** Aldehyde dehydrogenase 2 (ALDH 2) metabolizes acetaldehyde, the major cause of alcohol hangover symptoms. It also detoxifies lipid peroxidation-induced reactive aldehydes, such as 4-hydroxynonenal (4-HNE). Nonalcoholic steatohepatitis (NASH)- induced oxidative stress promotes lipid

peroxidation of cellular membrane, leading to the generation and accumulation of 4-HNE. This byproduct reacts with DNA to form highly carcinogenic exocyclic etheno-DNA adducts, potentially developing hepatocellular carcinoma. Recently, a variety of anti-hangover products are commercially available, however, almost none of them has been proven to show enhanced acetaldehyde-metabolizing capacity in a live subject.

**Aims & Methods:** We aimed to investigate a specific product of interest. The enzyme activities of the anti-hangover substance were examined by in-vitro & in-vivo experiments to measure the amount of NADH formation which is generated through catalytic conversion of alcohol and acetaldehyde, by using a spectrophotometer at 340 nm. Powder sample of a commercial anti-hangover product (South Korea) was used as the experimental substance. In-vivo examination tested the ethanol and acetaldehyde concentration in blood of rats with oral infusion of experimental substance before or after ethanol intake. In first test, twenty-four SD male rats were randomly assigned into one of four groups: group1 received only saline, group2 was subjected to ethanol only, group 3 received ethanol with substance (73 mg/kg), and group 4 ethanol with substance (220 mg/kg). Oral dosing of 50% ethanol (3 g/kg body weight) was given 30 minutes after substance gavages, followed by time-dependent collection of rat's blood when zero, 1, 3, 5, and 8 hours after dosing of ethanol. In second test, similar examination was repeated with two groups including ethanol only ($n = 6$) and ethanol with substance (220 mg/kg) ($n = 6$). The differentiator of second in-vivo test was that experimental substance be given 1 hr after ethanol gavage, approximately near maximum level of blood acetaldehyde.

**Results:** In vitro measurements of the activities of alcohol dehydrogenase & aldehyde dehydrogenase within the anti-hangover substance were 1.84 unit/g and 0.28 unit/g, respectively. The enzyme activities in rats' blood under the substance that was given 30 minutes before ethanol intake are as follows: after 1 hour of ingestion of ethanol, the concentration of ethanol in blood showed maximum values for all testing group, but decreases by 15.5% ($p < 0.246$) and 28.3% ($p < 0.011$) were observed for testing groups of dosing substance 73 and 220 mg/kg, respectively. In the case of a group with dosing 220 mg/kg, meaningful decrease in the concentration of ethanol through all measurement times was observed compared to a group of ingestion of ethanol only. With acetaldehyde level in blood, the maximum values for all testing groups were measured 1 hr after ethanol ingestion, demonstrating no significant differences among testing groups. However, the concentration of acetaldehyde in blood for ethanol only group started to decease after 3 hours, in contrast, those of groups with anti-hangover substance have shown concentration-dependent reduction after one hour. As for a group of dosing substance 220 mg/kg, meaningful level of decreases were observed after 3 hours ($p < 0.01$) and 5 hours ($p < 0.05$). Finally, the cases with oral intake of substance 220 mg/kg after 1 hr of ethanol intake have shown more significant and obvious decreases in blood acetaldehyde concentration through the period of all measurement times.

**Conclusion:** Oral intake of a specific anti-hangover substance has significantly enhanced alcohol and acetaldehyde-metabolizing capacity in rat model, potentially suggesting increased ALDH 2 capacity within circulation. Using this substance, further research on animal model of disease and detoxifying ability of other reactive aldehydes is recommended to conduct.

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### P1156 PROGNOSTIC ROLE OF 25-HYDROXYVITAMIN D IN PATIENTS WITH LIVER METASTASES FROM COLORECTAL CANCER TREATED WITH RADIOFREQUENCY ABLATION

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**Introduction:** Vitamin D is implicated in the etiology of several neoplastic diseases but its relationship with colorectal cancer survival is still unclear. Aim of this study was to determine whether vitamin D levels influence survival outcomes in colorectal cancer liver metastases patients treated with percutaneous radiofrequency ablation.

**Aims & Methods:** We measured 25-hydroxyvitamin D levels in 143 patients with 215 colorectal liver metastases who underwent radiofrequency ablation between 1999 and 2011 at our Institution. The influence of 25-hydroxyvitamin D levels on overall survival and time to recurrence was evaluated in univariate and multivariate Cox analyses.

**Results:** Median age was 68 years (range 41–85) and median number of nodules was 2 (1–3) with a median maximum diameter of 26 mm (10–48). Median survival was 44 months (36–62) and survival rate was 91.4%, 46.5% and 42.2% at 1, 4 and 5 years in the whole cohort. Median survival was 65 months (52–74) if 25-hydroxyvitamin D $>$ 20 ng/mL and 34 months (24–41) if $\leq$ 20 ng/mL ($p < 0.001$). In the whole cohort median time to recurrence was 34 months (26–47), 50 months (36–62) in the case of 25-hydroxyvitamin D $>$ 20 ng/mL and 24 months (20–32) if $\leq$ 20 ng/mL ($p < 0.001$). Nodule size and 25-hydroxyvitamin D resulted as significant predictors of both overall survival and time to recurrence in multivariate analysis.

**Conclusion:** Our study provides support for the use of 25-hydroxyvitamin D as a new predictor of outcome for colorectal liver metastases patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1157 ROLE OF MIR-122 EXPRESSION IN EVALUATION OF PROGNOSIS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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**Introduction:** New non-invasive diagnostic and prognostic biomarkers are needed to improve the clinical management of patients with hepatocellular carcinoma (HCC). Several studies, predominantly from Asian region, demonstrated differential expression of liver-specific microRNA miR-122 in tissue as well as in sera of patients with mostly HBV/HCV-induced HCCs. Therefore, miR-122 has been suggested as a biomarker for HCC.

**Aims & Methods:** In this study, we aimed to evaluate the prognostic value of miR-122 in patients with HCC in the European population and to determine potential factors related to miR-122 expression in serum. During the period of two years, we included 91 patients with confirmed HCC. Tumor staging was performed based on the BCLC-Classification. Clinical status and laboratory parameters (including AFP, ALAT, ASAT etc.) were assessed. Total RNA was extracted using miRNeasy kit. MiRNA expression analyses were performed using TaqMan qPCR for miR-122 normalized to a spiked-in cel-miR-39. Overall survival data were used to evaluate the prognostic value of miR-122.

**Results:** miR-122 showed a high interindividual expression variability in patients with HCC. Patients with different BCLC stages showed similar miR-122 expression in serum. In similar fashion, no significant differences were found neither for the Child-Pugh-Stage nor for the etiologically underlying liver disease. Overall, we observed positive correlation between the miR-122 in serum and parameters such as ALAT ($p < 0.0001$), ASAT ($p = 0.0001$), AFP ($p = 0.0034$) and hemoglobin concentration ($p = 0.0076$). A negative correlation was observed for creatinine concentration ($p = 0.0028$). Subsequently, miR-122 expression was higher in patients with pathological ALAT-, ASAT- or AFP-values; while significantly lower in patients with impaired renal function measured by creatinine concentration. Despite the correlation to liver-/tumor-related laboratory parameters, miR-122 level variation in serum was not associated with the survival of patients with HCC.

**Conclusion:** miR-122 expression in sera from patients with HCC strongly correlated with AFP and liver enzymes. Furthermore, miR-122 concentration seems to be influenced by renal function and hemoglobin concentration. However, we could not observe a significant prognostic value of miR-122 in sera of HCC patients with predominantly alcohol-induced liver damage.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1158 SORAFENIB IN CLINICAL PRACTICE: POOLED ANALYSIS OF TWO PROSPECTIVE OBSERVATIONAL STUDIES IN HEPATOCELLULAR CARCINOMA (HCC)

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**Introduction:** Sorafenib is the recommended standard of care in HCC patients with preserved liver function who are ineligible or have failed surgical or loco-regional treatments.

**Aims & Methods:** Characterize efficacy and safety of sorafenib in routine clinical practice in Italian centers. Data from the Italian subgroup of GIDEON (international study) and from STELLA (Italian study), two prospective observational studies were pooled. Efficacy and safety of sorafenib were primary objectives in the two studies. Eligible patients were those for whom the decision to treat with sorafenib has been made prior to enrollment.

**Results:** Between June 2009 and January 2014, 512 patients were enrolled in both studies of which 498 were valid for efficacy and 485 for safety analysis. Demographic characteristics: male 81%, median age 70y (range 28–90) and $>$26% 75y or above. Etiology: hepatitis C in 55% and hepatitis B in 20% of patients. The majority (62%) had ECOG PS 0 and Child-Pugh A/B/C was present in 79/13/1% respectively. More than half of patients were BCLC stage C (58%) whereas BCLC B and BCLC A accounted for 31% and 9% respectively. Overall incidence of adverse events-(AE) (all grades) was 82%. The most frequent were fatigue (29%), diarrhea (24%) and hand-foot skin

reaction (16%). Incidence of AEs resulting in permanent discontinuation (drug-related or not) was 32%. Median overall survival was 10.7 [95%CI:9.3–12.7] months and median time to progression was 6 [95%CI:5.2–7.0] months.
**Conclusion:** This pooled analysis represents the largest prospective database of patients treated with sorafenib in routine clinical practice in Italian centers and confirms the efficacy and safety data of the phase III registrational studies. The use of sorafenib in the advanced as well as in the intermediate and early stage HCC confirms its role in the continuum of care of HCC patients and the treatment stage migration approach in clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1159 IMPROVING SURVIVAL OF PATIENTS WITH HEPATOCELLULAR CARCINOMA BETWEEN 2005 AND 2012 IN THE FINISTERE AREA

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**Introduction:** Relevant diagnostic procedures and advanced treatments have been introduced in the management of hepatocellular carcinoma (HCC)
**Aims & Methods:** The aim of the study was to assess the effect of treatment procedures evolution on survival between 2005 and 2012 in the Finistere area. All cases of HCC (n = 971) diagnosed from January 1st, 2005, throughout December 31st, 2012, were registered in the database of the Finistere registry of digestive cancers. Diagnostic circumstances, medical background, type of diagnosis confirmation, Child-Pugh score and BCLC staging classification, treatment and AFP levels have been tested for their effect on survival. Patients were divided into two groups according to the diagnosis date. The 5-year cancer specific survival (CSS) was calculated by Kaplan-Meier method and a multivariate analyse by cox model.
**Results:** Overall, the 5-year CSS significantly increased during this 8-year period, from 12.9% for cases diagnosed between 2005 and 2008 to 21% for cases diagnosed from 2009 onward ($p < 0.05$). Patients diagnosed during screening procedures had a 5-year survival rate of 25.5% vs 7.6% in case of symptomatic diagnosis ($p < 0.001$). They underwent more curative or interventional treatment in 67.0% of cases whereas it dropped to 22.2% in case of symptomatic diagnosis. We observed a strong association between the AFP level and prognosis, CSS being 25.9 months (IC95 20.5–30.8) for AFP level below 14 ng/mL, as compared with 9.7 months (IC95 7.3–11.5) and 3.1 months (IC95 2.6–3.8) for levels between 14 and 199 ng/mL or above 200 ng/ml respectively. In the multivariate analysis, clinical presentation, tumor size, AFP level, Child-Pugh score, BCLC stage and treatment were independent prognostic factors for the 5-year CSS.
**Conclusion:** Cancer specific survival rate significantly increased during this 8-year period in HCC patients, mostly in patients diagnosed during screening. A low level of AFP is a significant prognostic factor.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1160 SURVEILLANCE FOR HEPATOCELLULAR CARCINOMA (HCC): A CLINICAL AUDIT

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**Introduction:** AASLD and EORT guidelines recommend 6-monthly ultra-sound surveillance for the detection of hepatocellular carcinoma in patients with cirrhosis[1,2]. Our previous audits showed that compliance with ultrasound surveillance remains unsatisfactory despite patients' involvement and consent, using our previous paper based recall system[3]. We aim to check our compliance rate of six monthly surveillance ultrasound scans (USS) following implementation of our recall system using Excel.
**Aims & Methods:** All patients known to CLC until end Dec 2015 were audited. Cirrhosis was confirmed by liver biopsy, Fibroscan, ELF test or a shrunken liver in the clinical setting. Comparison was made with audit data from 2012 and 2014. A database of all patients with cirrhosis was constructed and their details entered into an Excel spreadsheet. USS surveillance was requested upon receipt of a non-significant report and the patient informed. For patients with a significant report, further investigation was organised and an early outpatient review was made. Using the Excel spreadsheet date function, the patient was sent a reminder letter if s/he did not attend USS when due.
**Results:** Compliance rate for previous audit years 2012 and 2014 were 26% and 56% respectively. There were 423 patients in total. 256 were male and 167 were female. 92 patients were excluded: 63 patients died, 25 patients moved to another hospital or consultant and 4 declined surveillance. Of the 331 remaining patients (205 male, 126 female; ratio 1.6:1) we found that: 236 (71.3%) had a surveillance USS within the last 6 months 95 (28.7%) did not attend the appointment
Females complied better with surveillance; 138 (67.3%) of males attended versus 98 (77.8%) of females who attended.
**Conclusion:** Our results show that our rate of compliance has improved over the years and following the introduction of a departmentally designed recall and reminder system using a standard off the shelf Excel program. To further improve our compliance, we are planning a telephone appointment reminder aimed especially at patients who are recurrent non-attenders with a subsequent re-audit of results in a further 1 to 2 years.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1161 VIRTUAL PALPATION MODEL BASED ON SPIRAL CT AND ELASTOGRAPHY DATA - PROOF OF CONCEPT

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**Introduction:** Palpation is a skill that has been increasingly neglected over recent years due to the advent of numerous new technologies that facilitate diagnosis. However, it remains one of the four pillars of proper clinical investigation and is a prequisite in all medical schools worldwide. It traditionally involves direct contact with the outer layers of the body, therefore being restricted to organs in close contact to adjacent structures.
**Aims & Methods:** Our aim was to implement modern imaging data combined from computed tomography (CT) and real-time elastography (RT-E) and Fibroscan in a haptic simulator capable of reproducing a virtual deformable model of a liver tumor. We have obtained ethical clearance from the local committee and obtained informed consent from 25 patients scheduled for surgery with hepatocellular carcinomas. All patients underwent CT scans as part of their medical work-up, as well as liver elastography and Fibroscan for obtaining elastographic data of the tumor. By using previously described methods [1] we created a three-dimensional model of the liver and the tumor using the CT data and integrated elasticity information by superimposing the RT-E and Fibroscan data on the stiffness of each tumor, obtaining virtual models containing segmented color-map data superimposed on high-fidelity representations of the tumors. This three-dimentional rendering was integrated in a virtual reality system and we used a haptic device to simulate direct contact. A test group of 120 medical students that already completed the Gastroenterology course was presented with the model and asked to complete a survey after using the device for 1

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| | Strongly disagree | Disagree | Partially agree | Agree | Strongly Agree |
|---|---|---|---|---|---|
| The model is accurate in size | 0 | 0 | 5 | 18 | 97 |
| The model is accurate in shape | 0 | 0 | 6 | 27 | 87 |
| The model is accurate in location | 0 | 0 | 8 | 31 | 81 |
| The model is easily maneuverable | 0 | 0 | 1 | 24 | 25 |
| The haptic device provides accurate interaction with the virtual model | 0 | 5 | 31 | 12 | 72 |
| The virtual reality glasses provided an adequate experience | 0 | 3 | 21 | 12 | 84 |
| The system is easy to use | 0 | 1 | 3 | 46 | 70 |
| The interface is user-friendly and intuitive | 0 | 0 | 6 | 55 | 59 |
| The system provided useful insight on the characteristics of liver tumors | 0 | 0 | 0 | 14 | 106 |
| The system effectively increased knowledge on the studied pathology | 0 | 0 | 0 | 0 | 120 |

hour each. They also had access to data on the real tumor (size, shape and location).
**Results:** The results to the survey are presented in the table below. According to the survey answers, all students considered the model to be accurately depicted by the three dimensional rendering. They found the system to be useful and to increase knowledge on liver malignancy, providing insight otherwise unobtainable through standard teaching methods. The system, however, was not easy to operate and did not provide an accurate interaction for all students.
**Conclusion:** We have continued our previous work by expanding the capabilities of a haptic device used to facilitate virtual palpation of a liver tumor. Medical training should include modern techniques in an approachable manner, facilitating direct contact between the student and the studied pathology. The results of our survey proved that such systems increase knowledge on liver tumors.
**Disclosure of Interest:** C.T. Streba: Supported by Partnership Project No. 2011–3.2–0503, VIPsystem
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All other authors have declared no conflicts of interest.

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### P1162 DIAGNOSTIC PERFORMANCE OF PIVKAII AND NEW POTENTIAL SERUM BIOMARKERS GP3, CSTB, SCCA1 AND HGF FOR DIAGNOSIS OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS

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**Introduction:** Biomarkers have the potential for early detection of disease translating to better management. Concerning the great burden of chronic liver disease (CLD) and hepatocellular carcinoma (HCC), biomarkers for the detection of HCC have great potential to change the management and prognosis of patients with CLD and HCC.
**Aims & Methods:** The aim of the study was to investigate diagnostic performance of Protein induced by vitamin K absence or antagonist-II (PIVKAII) and new candidates Glypican-3 (GP3), Cystatin B (CSTB), Squamous cell carcinoma antigen 1 (SCCA1) and Hepatocyte growth factor (HGF) as potential biomarkers for hepatocellular carcinoma (HCC) in patients with alcoholic liver cirrhosis (ALC). Eighty two participants were included: 19 healthy volunteers, 31 patients with ALC and 32 patients with HCC. Peripheral blood sampling was performed for each participant and serum levels of PIVKAII, GP3, CSTB, SCCA1 and HGF were analyzed using commercial ELISA kits. Patients were excluded if they were younger than 18, had prior treatment of HCC, history of other solid tumour, or elevated serum creatinine level.
**Results:** Only serum levels of PIVKAII were significantly higher in HCC patients as compared to ALC and healthy controls (cut-off 2.06 ug/L; AUC 0.903), whereas diagnostic performance of other individual compounds and their combinations was suboptimal. All tested compounds had significantly higher serum levels in cirrhotic patients as compared to healthy controls. Moreover, significant increase in serum concentration of GP3, CSTB and SCCA1 (all $p < 0.01$) was observed along progressive Child-Pugh stages of cirrhosis, whereas CSTB and SCCA1 expressed moderately strong correlation ($r2 = 0.6$ and 0.65 respectively, both $p < 0.001$) with liver functional stage expressed by MELD score.
**Conclusion:** With the exception of PIVKAII, examined biological compounds had suboptimal diagnostic performance for HCC in ALC. Obtained results might indicate CSTB and SCCA1 as potential non-invasive biomarkers of liver function and cirrhosis development which should be further investigated.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1163 MIRIZZI SYNDROME: HOW TO MANAGE

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**Introduction:** Mirizzi syndrome (MS) is a rare complication of cholelithiasis. The Mirizzi Syndrome (MS) is characterized by impaction of gallstone in either the cystic duct or the Hartmann pouch of the gallbladder, resulting in compression of the adjacent common hepatic duct **(1).** It has been extending to patients in whom there is an erosion of the gallbladder wall or cystic duct so that it communicates with the bile duct, forming a cholecystocholedochal fistula **(2,3)**. This entity should be considered in the differential diagnosis of all patients with obstructive jaundice. Failure to recognize this condition preoperatively can result in a major bile duct injury. In this study, our aim is to describe the clinical presentations, investigations, operative details, endoscopic management and the complications of both procedures.
**Aims & Methods:** We performed a retrospective analysis on the records of 85 patients with MS. All patients had a cholangiogram either; magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP). We used a McSherry classification to divide patients with MS into type I MS and type II MS.
**Results:** The incidence of MS was 0.98% from a total of 4620 patients who had undergone cholecystectomy. From 85 patients with MS 30 patients underwent ERCP where it was the sole treatment (28 of which had stent while 2 had the stone extracted). The overall surgically treated patients were 55 (28 patients with preliminary ERCP with stent and 27 patients with primary surgical treatment), 28 patients had MS type I while 27 patients had MS type II. Patients with different types of MS underwent different types of surgical procedure.
**Conclusion:** Surgery is the mainstay of therapy of Mirizzi syndrome, and requires the safe completion of cholecystectomy and the appropriate management of the cholecystocholedochal fistula. Endoscopic treatment may be effective as a temporary measure before surgery and can be definitive treatment for unsuitable surgical candidates.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1164 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:** Although endoscopic transpapillary gallbladder drainage (ETGBD) has been reported to be an effective treatment for acute cholecystitis, it may not be technically feasible in difficult cases. As an alternative, endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) has been introduced as a safe and effective method for drainage of the gallbladder.
**Aims & Methods:** The aim of this study was to compare the outcomes of EUS-GBD and ETGBD. Retrospective review of a prospectively collected endoscopic gallbladder drainage database at the Asan Medical Center (From January 2010 to December 2014) was performed to identify consecutive patients with acute cholecystitis who underwent attempted endoscopic gallbladder drainage for decompression of the gallbladder. A total of 179 patients (83 in EUS-GBD group and 96 in ETGBD group) who had undergone either EUS-GBD or ETGBD for acute cholecystitis were included. The inclusion criteria were: 1) acute cholecystitis, 2) advanced malignancy and/or poor surgical performance (class III or IV on the American Society of Anesthesiologists Physical Status classification system).
**Results:** Technical success rate (EUS-GBD vs. ETGBD group; 98.8% (82/83) vs. 83% (80/96), $P < 0.05$) and clinical success rate (EUS-GBD vs. ETGBD group; 95.2% (79/83) vs. 83% (80/96), $P < 0.05$) were significantly higher in EUS-GBD group than ETGBD group. There was no significant differences in the mean procedure time (EUS-GBD vs. ETGBD group; $21 \pm 6.2$ minutes vs. $19.5 \pm 9.6$ minutes, $P = 0.22$) and procedure-related adverse event rate (EUS-GBD vs. ETGBD group; 8.4% (7/83) vs. 8.3% (8/96), $P = 0.74$). In the EUS-GBD group, procedural adverse events included self-limitied pneumoperitoneum (3/83, 3.6%), self-limited abdominal pain (3/83, 3.6%), and duodenal perforation (1/83, 1.2%). In the ETGBD group, post-procedural pancreatitis occurred in 8 patients (8.3%). All procedure-related adverse events resolved with conservative treatment. During the follow-up periods, acute cholecystitis recurred more frequently in ETGBD group (EUS-GBD vs. ETGBD group; 7.2% (6/83) vs. 17.7% (17/96), $P = 0.02$) As a result, re-intervention was more frequently needed in ETGBD group (EUS-GBD vs. ETGBD group; 7.2% (6/83) vs. 17.7% (17/96), $P = 0.02$).
**Conclusion:** In patients with acute cholecystitis and unfit for surgery, EUS-GBD might be more useful treatment method than ETGBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1165 BILE DUCT STONES RECURRENCE AFTER ESWL IN THE ELDERLY: PREDICTIVE FACTORS

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**Introduction:** Extraction of ductal stones via endoscopic biliary sphincterotomy may be complex, the most frequent reason is stone size greater than 15 mm[1]. Extra-corporeal shock wave lithotripsy (ESWL) can be considered in difficult bile duct stones (DBDS) with a success rate greater than 90%[2] but data about the recurrence rate of common bile duct stones after ESWL are limited.
**Aims & Methods:** From May 1992 to October 2012, patients who underwent ESWL treatment for DBDS, not amenable to endoscopic extraction, were included. Patients who had undergone liver transplantation or choledochotomy were excluded. Clinical information was retrospectively reviewed, and data about long-term outcome were collected through phone interviews and medical records. Chi square test and Mann-Whitney test were used to study significant differences between patients with or without bile duct recurrence. Subsequent multivariate analysis on significantly different variables was performed by means of logistic regression. The accuracy of the identified predictors of recurrence was evaluated with ROC curve analysis.
**Results:** A total of 202 patients (median age 77 years, range 41–95) with a successful clearance of DBDS after ESWL were included. 85 had gallbladder stones, while 112 underwent cholecystectomy before the DBSD diagnosis or within a month from the last ESWL session. During a median follow-up period of 4.64 years, 40 patients (20%) developed a recurrence of bile duct stones with biliary colic in 18 patients, cholangitis in 15, acute pancreatitis in 2 and asymptomatic in 5. As expected, there was a significantly higher number of patients with gallbladder stones (60% vs 38%, $p = 0.0185$) and not cholecystectomized (60% vs 40%, $p = 0.0395$) in the recurrence group. Mean diameter of stones ($2.458 \pm 0.96$ vs $2.089 \pm 0.710$, $p = 0.0315$) and of the common bile duct were significantly higher in the recurrence group. Logistic regression analysis confirmed that the common bile duct diameter (OR 1.42; 1.19–1.71, $p = 0.0001$) and the maximum stone diameter (OR 1.90, 1.19–3.03, $p = 0.0065$) were significantly associated with recurrence. Interestingly, ROC curve analysis identified a main bile duct diameter of $> 10$ mm to be associated with recurrence (sensitivity 92.5%, $p < 0.0001$).
**Conclusion:** In our elderly population we observed a recurrence of 20% over a median follow-up of 4 years. This study confirms that the presence of stones in the gallbladder is a risk factor for bile duct stone recurrence as well as stone size. However, the common bile duct diameter associated with a higher risk of recurrence is lower than what has been previously published[3], a data that may impact on clinical decisions in elderly fit subjects.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1166 PROCHOLESTATIC GENE VARIANTS AND MUTATIONS IN SECONDARY SCLEROSING CHOLANGITIS IN CRITICALLY ILL PATIENTS (SC-CIP)

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**Introduction:** Secondary sclerosing cholangitis in critically ill patients (SC-CIP) has been recently defined as new disease entity. The pathogenesis of SC-CIP is unclear, however ischemia and "toxic bile" might be involved.
**Aims & Methods:** It was our aim to study selected procholestatic gene variants and mutations in patients who developed secondary sclerosing cholangitis (SSC) after an intensive care unit (ICU) stay. In total, we screened data of 4,641 cholangiography procedures performed between January 2008 and April 2015 at Saarland University Medical Center. In total, we identified 17 patients (age 33–80 years, 14 males) with a history of ICU treatment and signs of SSC. In these patients, we retrospectively analyzed the data concerning ICU therapy. In all patients we genotyped the following procholestatic mutations (marked with an asterisk) and polymorphisms: ATP8B1 (p.N45T*, p.E429A*, p.I661T*, p.R952Q), ABCB4 (p.R590Q*, c.787 A > T, c.504 T > C), ABCB11 (p.E297G*, p.A444V, p.D482G*, c.3084A > G), and FXR (c.-1 G > T). The genotype frequencies were compared with data from reference populations.
**Results:** Among the SC-CIP patients, myocardial infarction ($n = 5$, 29%) was the most common reason for the ICU stay, followed by cardiac surgery, pneumonia, and polytrauma ($n = 3$, respectively). The first endoscopic retrograde cholangiography procedure was performed on an average of 105 days (range 24–1155 days) after the ICU treatment. All patients presented with increased cholestatic markers (median bilirubin 3.5 mg/dl, gamma-GT 731 U/l, alkaline phosphatase 428 U/l). All SC-CIP patients had infectious complications during their ICU stay. In 6 of 8 patients with cholangitis, microbiological analysis of bile revealed *Entercoccus faecium* (66.7%) and *Enterococcus faecalis* (50.0%) species; a single patient tested positive for Candida species. The disease progressed to liver cirrhosis in 8 (47%) patients, two received liver transplantation, and three patients died (17.6%).One patient was a heterozygous carrier of the FXR c.-1 > t mutation. Otherwise, we did not detect any differences in ABCB4, ABCB11 and ATP8B1 genotype distributions as compared to the general population.
**Conclusion:** To our knowledge this is the first study investigating hepatobiliary transporter variants in patients with SC-CIP. Although our preliminary results do not indicate an association between the gene variants and SC-CIP development, a more comprehensive approach (next-generation sequencing) is required to fully explore the impact of rare gene variants on SC-CIP risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1167 PREDICTORS FOR DETECTION OF DIFFICULT-TO-TREAT BACTERIA IN BILIARY TRACT INFECTION

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**Introduction:** Empiric antimicrobial therapy for severe bacterial infection should sufficiently cover the possible causative pathogens. For this purpose, it is important to accurately predict the causative microbes. However, few studies have revealed the relation between host factors and causative bacteria in biliary tract infection.
**Aims & Methods:** We aimed to determine the patient factors which predict detection of difficult-to-treat bacteria (DTTB) as pathogens of biliary tract infection. A hundred and twenty-three cases of bacteraemia derived from biliary tract infection treated in our hospital between January 2010 and September 2015 were included. We examined the relation between the detection of DTTB and the patient factors, such as age, sex, biliary tract malignancy, complication, timing of bacteraemia, severity, device in the biliary tract, immunosuppressive therapy, loss of the sphincter function of the papilla, history of hospitalization within 30 days, use of antibiotics within 3 months and history of DTTB detection. We defined DTTB as extended-spectrum beta-lactamase (ESBL)-producing organisms, metallo-beta-lactamase (MBL)-producing organisms, a group of "SPACE" (which stands for *Serratia*, *Pseudomonas*, *Acinetobacter*, *Citrobacter*, and *Enterobacter*), and ampicillin-resistant enterococci.
**Results:** DTTB were detected in 28 cases (22.8%). Univariate analysis revealed that the factors significantly correlated to DTTB detection were the following: biliary tract malignancy (32.6% vs 16.9%, $p = 0.04$), loss of the sphincter function (37.9% vs 18.1%, $p = 0.03$), history of hospitalization (35.3% vs 18.0%,

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Table 1

| Animal | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Technical success | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Procedure duration (minutes) | 35 | 37 | 28 | 17 | 19 | 15 | 14 | 16 | 20 | 19 |
| Time of acrifice (hours/days) | 6 h | 24 d | 10 d | 21 d | 42 d | 42 d | 42 d | 42 d | 1 h | 1 h |
| Complications | None | None | None | None | None | None | None | None | None | None |
| Migration of the stent | No | No | No | No | Yes | No | Sham procedure | Sham procedure | No | No |
| Gallbladder status on ERCP | Normal | Normal | Normal | Normal | Normal | Normal | Normal | Sludge in the gallbladder | Normal | Normal |
| Device conditions at autopsy | Normal | Normal | Normal | Normal | Normal | Normal | Not implanted | Not implanted | Normal | Normal |

p = 0.04), resent use of antibiotics (37.8% vs 16.3%, p < 0.01), and history of DTTB detection (42.1% vs 19.2%, p = 0.04). In multivariate analysis, only resent use of antibiotics was significantly correlated to DTTB detection (P < 0.01).
**Conclusion:** Resent use of antibiotics increases the possibility of DTTB detection in biliary tract infection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1168 A NOVEL NITINOL GALLBLADDER STENT FOR PREVENTION OF STONE MIGRATION AND IMPACTION

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**Introduction:** Up to 20% of western populations have gallstones. Cholecystectomy is the standard treatment with 2 million procedures annually worldwide. Although safe and routinely performed, cholecystectomy can lead to complications and even death 1. Gallstones become a problem requiring intervention only when they block bile flow from the galblladder or migrate into the bile ducts. The LithoBlocker™ is a patented nitinol umbrella-like stent, designed to prevent gallstones from blocking the orifice of the gallbladder and from migration into bile ducts, while maintaining gallbladder function, as well as free bi-directional bile flow. The stent accomodates itself within the gallbladder facing its orifice upon release from the delivery system.
**Aims & Methods:** The LithoBlocker™ is inserted into the gallbladder during a standard ERCP procedure using a conventional metalstent delivery system. The aim of the present study was to investigate the feasibility and safety of insertion and deployment of the stent into the gallbladder of pigs. In addition, short-term safety of the stent was evaluated.
**Results:** The study protocol was approved by the hospital ethical committee. ERCP was done in 10 animals at the facility of the Catholic University of Rome, Italy. The mean weight of the animals was 35 kg. Before ERCP the animals were held on an overnight fast and abdominal ultrasound was done to determine the size of the gallbladder (to choose the stent size) and to exclude any unexpected anatomical abnormalities. After ERCP, the animals were held at the facility, allowing water and food ad libitum. The animals were sacrificed at the end of the follow-up period. The procedures were performed with a standard Olympus duodenoscope (TJF 140) under fluoroscopic control and general anesthesia. After biliary cannulation, cholangiography and sphincterotomy, the gallbladder was cannulated with a hydrophilic guidewire through the cystic duct. The LithoBlocker™ device was introduced over the same guidewire into the gallbladder with an 8Fr or 8.5 Fr introducer catheter. The stent (available between 4–8 cm in length) was deployed in the gallbladder under fluoroscopy. A total of ten procedures, 8 device placements and 2 sham procedures (complete procedure with contrast injection, sphincterotomy, insertion of guide wire and delivery system into the gallbladder without stent deployment) were performed. Data are shown in Table 1. No procedure or device related complications were observed. The mean procedure time was 20.5 minutes (14–37). The maximum follow-up until sacrifice was 42 days. On autopsy, the stent was correctly in place in 7 pigs, while it migrated completely in 1.
**Conclusion:** The LithoBlocker™ can be easily introduced into the gallbladder by a standard ERCP procedure, without any immediate or short term complications. It is a promising tool that could prevent gallstone migration and impaction. Clinical trials are warranted to confirm these results.
**Disclosure of Interest:** F. Konikoff: Prof. Konikoff is a medical director at Lithiblock
S. Ben Muvhar: Founder and CEO at Lithiblock. Financial support for the study done at the animal facility of the Catholic University of Rome, Italy
J. Tsehori: Dr. Tsehori is a cofounder of Lithiblock
All other authors have declared no conflicts of interest.

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## P1169 RELATIONSHIP BETWEEN GALLBLADDER STONE AND CARDIOVASCULAR DISEASE RISK

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**Introduction:** Cardiovascular disease (CVD) and gallstones are among the most common diseases in the society and share common risk factors. Our aim is to determine whether there is an increase in 10-year CVD risk in the patients with gallstones and whether gallstone is a risk factor for cardiovascular disease.
**Aims & Methods:** We analyzed 90 patients diagnosed with gallstones disease and 72 healthy subjects without gallstones. Demographic and laboratory data were collected, Framingham risc scores were calculated and both groups were compared for the 10-year CVD risk. Then, demographic and laboratory data of individuals who had moderate-severe risk and low risk for CVD were compared. Moreover, multivariate logistic regression analyses were performed and ORs with 95%CI were calculated in order to indentify the risk factors of CVD.
**Results:** 10-year CVD risk is significantly higher in cases with gallstone disease than without gallstones (p:0.005). In the cases having moderate- severe risk for CVD, total cholesterol, systolic blood pressure, hematocrit etc. were significantly higher acording to the cases with low risk (Table-2). In the results of multivariate logistic regression analyses, 7,8-fold increase in the risk of CVD was found in the patients with gallbladder stone. Odds ratio of other possible risk factors in the increased risk of CVD risk are given in Table 2.
**Conclusion:** At the end of the study; it was found that gallstones were associated with a high risk of cardiovascular disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Table-2:** Between group comparisons and logistic regression results according to Framingham risc groups

| Variable | Between group comparisons Low risc (n:94) | Logistic regression analysis Moderate-severe risc (n:68) | P value | **Multivariate Odds Ratio (95%CI)** | **P value** |
|---|---|---|---|---|---|
| Age (yr) | 45 (40–51) | 60 (52.5–67) | <0.001 | 1.3 | <0.001 |
| Gender (female/male) | 84(%89.4)/10 (%10.6) | 31 (%45.6)/37 (%54.4) | <0.001 | 178.7 | <0.001 |
| Smoke | 9 (%9.5) | 26 (%38.2) | <0.001 | - | - |
| Diabetes | 15 (%15.9) | 29 (%42.6) | <0.001 | 6.6 | 0.04 |
| Hypertension | 19 (%20.2) | 39 (%57.3) | <0.001 | - | |
| BMI ($kg/m^2$) | 31.1 (27.7–35.4) | 32.1 (27.9–36.2) | 0.41 | 1.1 | 0.07 |
| T.cholesterol (mg/dl) | 192.54 ± 39.73 | 217.45 ± 45.94 | <0.001 | - | - |
| Htc (%) | 39 (34.5–41.8) | 42 (37.8–44.6) | <0.001 | | |
| Systolic (mm Hg) | 117.5 (110–130) | 135 (121.2–150) | <0.001 | 1.1 | <0.001 |
| Diastolic (mm Hg) | 70 (60–80) | 80 (70–90) | 0.002 | - | - |
| AST (IU/L) | 18 (14.7–22) | 20 (17–29.2) | 0.003 | - | - |
| ALT (IU/L) | 16 (13–26) | 21.5 (14–42) | 0.019 | - | - |
| Creatin (mg/dl) | 0.73 (0.64–0.82) | 0.85 (0.75–1.02) | <0.001 | - | - |
| LDL (mg/dl) | 121.5 (91.7–138) | 139 (119–153.5) | <0.001 | 1.1 | <0.001 |
| HDL (mg/dl) | 44 (38–52) | 40 (32–46) | <0.001 | 0.85 | 0.002 |
| TG (mg/dl) | 118.5 (95.2–160.2) | 157.5 (126.5–210.7) | <0.001 | - | - |
| Platelet ($10^3 \mu L$) | 257.5 (205–305.5) | 238.9 (207.2–287) | 0.13 | - | - |
| WBC ($10^3 \mu L$) | 6.99 (5.75–8.65) | 7.3 (6.3–9.3) | 0.12 | - | - |
| Group-1 | 44 (%46.8) | 46 (%67.6) | 0.008 | 7.8 | 0.017 |

Values are expressed as n (%), mean ± SD or median(25th-75th percentiles). Htc: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BMI: Body mass index; HDL: High density lypoprotein; LDL: Low density lypoprotein; TG: Triglyceride; WBC: White blood cell

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## P1170 LAPAROENDOSCOPIC RENDEZVOUS FOR TREATING CHOLELITHIASIS WITH CONCOMITANT CHOLEDOCHOLITHIASIS UNSUITABLE FOR LCBDE


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**Introduction:** Choledocholithiasis is reported to accompany with cholelithiasis in 10–15% patients. The two-stage approach is widely applied: endoscopic etrograde cholangiopancreatography (ERCP) and common bile duct (CBD) clearance by laparoscopic cholecystectomy. Recent studies demonstrated laparoscopic management of CBD stones with choledochoscope-assistanted laparoscopic CBD exploration (LCBDE), as a single stage procedure, might be efficient and cost effective. For some ERCP-failed cases, intraoperative ERCP (IO-ERCP) using the laparoendoscopic rendezvous technique followed by laparoscopic cholecystectomy (LC) was effective and safe. It's still controversial for defining the ideal treatment of CBD stones. Rare reports showed the recommended strategy for patients not suitable for LCBDE with the choledochoscope assistance. Our aim was to evaluate the advantage of IO-ERCP combined with laparoendoscopic rendezvous in these cases.
**Aims & Methods:** For the patients suspected cholelithiasis with concomitant choledocholithiasis, Magnetic Resonance Cholangiopancreatography (MRCP) was performed to assess the CBD diameter and stone number. Acquired the written informed consent, patients were cured by cholecystectomy and LCBDE with the choledochoscope assistance if no contraindications. IO-ERCP and laparoendoscopic rendezvous would be applicable for exploring CBD and cleaning stones while the CBD diameter was $<1$ cm and the stone number was $<3$. The cannulation was performed, and the stones was cleared by Dormia basket or balloon. Endoscopic nasobiliary drainage (ENBD) was carried out routinely, and removed due to no infection, no pancreatitis and no discomfort, which should be confirmed by clinical manifestation and blood tests after oral diet. For all patient, baseline characteristics, operation procedure, complication, hospitalization period and costs were recorded and compared.
**Results:** From Dec 20, 2014 to Sep 15, 2015, a total of 10 patients received the management of combining IO-ERCP and LC. Male/Female was 4/6. The mean diameter of CBD was 0.85 cm (0.7–1.0). The average number of stones was 2.1 (1–3). The average operation time was 120.8 min (98–154 min). No PEP or sever complications occurred. Patients were discharged after 4.8-day (3–7) hospitalization and the average costs were 35.000 RMB (33.000–38.000 RMB).
**Conclusion:** Combining IO-ERCP and LC for patients with these indications was efficient, safe and cost effective. Cooperating management ensured the successful cannulation, even without radiography. This innovative strategy could reduce the sphincter damnification, avoid post-operative stricture of CBD and prevent the PEP occurrence. For future clinical application, randomized controllable trials should be designed to demonstrate the superiority of this method.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1171 CLINICAL IMPACT OF PER-ORAL DIGITAL CHOLANGIOSCOPY (SPYGLASS) – A SINGLE CENTER EXPERIENCE


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**Introduction:** A new single-operator digital cholangioscopy (d-SOC) has recently been introduced in the clinical practice. In contrast to the 1st fiberoptic generation, it provides better imaging quality and superior maneuvaribility. Initial reports with 1st generation demonstrated low/intermediate diagnostic accuracy for visual diagnosis as well as for targeted biopsies under visual control in patients with indeterminate biliary strictures*.
**Aims & Methods:** The aim of our retrospective analysis was to assess the diagnostic accuracy and clinical impact of SOC, and of a digital version in particular, in patients with undetermined biliary strictures and in patients with difficult choledocholithiasis. Procedural success was defined as an ability to (1) visualize target lesions and collect biopsy specimens for histological evaluation, if indicated, and (2) achievement of a complete duct clearance.
**Results:** A total of 44 procedures (22 digital) were performed in 42 patients, 36 (86%) patients underwent cholangioscopy for diagnostic purposes and 6 (14%) for laser litothripsy. Overall, sensitivity, specificity and diagnostic accuracy in patients with undetermined biliary stricture was 90.0%, 88.2% and 88.9% respectively. First generation of SOC achieved sensitivity, specificity and diagnostic accuracy of visual impression 87.5%, 92.3% and 68.8%, while digital SOC achieved sensitivity and specificity 100%. Overall diagnostic yield of targeted biopsies for both generations was 78.6% (95% CI. 60.5–89.8%). The sensitivity of Spybit histology for the first generation SOC was 20% (95% CI 2.52-55.61%), the sensitivity of second generation Spybit histology was 100% (95%CI 15.8 – 100%) with no statistical difference ($p=0.5$ – chi square with Yates correction – low counts). All laser lithotrypsies ($n=6$) were performed by using a new d-SOC system and we achieved a complete duct clearance with stone removal in one session was accomplished in 5/6 patients (83%). Non-fatal adverse events occurred in a total of 8 patients (cholangitis, mild post-procedural pancreatitis, liver hematoma, bleeding) and occurred during diagnostic cholangioscopies with a similar frequency in d-SOC and the first generation SOC.
**Conclusion:** We observed a trend for improved both diagnostic accuracy and diagnostic yield of targeted biopsies with a new generation of digital single operator per oral cholangioscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1172 A PROSPECTIVE STUDY OF THE CLINICAL EFFICACY AND EFFECT OF PHOTODYNAMIC THERAPY FOR THE TREATMENT OF UNRESECTABLE EXTRAHEPATIC CHOLANGIOCARCINOMA


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**Introduction:** Photodynamic therapy (PDT) combined with stent placement is considered an effective palliative treatment for unresectable extrahepatic cholangiocarcinoma (EHCC). However, the available evidence is still insufficient and not yet strong enough for prospective, controlled study results reported infrequently [1–2]. The time interval between PDT procedures was no standardized recommendation. It remains unclear whether PDT plays a role in promoting a systemic inflammatory response in patients with EHCC.
**Aims & Methods:** This study aimed to explore the clinical efficacy and effect of this treatment on tumor tissues and the systemic inflammatory response in patients with EHCC. Patients with unresectable EHCC underwent either a combined treatment of PDT and stent placement (PDT+stent group, 12 patients) or stent-only treatment (stent group, 27 patients). Thickness of the tumor mass was measured using intraductal ultrasonography (IDUS) in every 3 months. TNF-$\alpha$ and IL-6 levels were determined 1 week pre- and postoperatively. Quality of life was assessed using Karnofsky performance scale (KPS) scores every 3 months.
**Results:** Average jaundice alleviation time was significantly lower in the PDT+stent group (19.7 (7–28) vs. 28.9 (13–45) d, $p=0.03$). Average survival time [13.8 (6.2–16.5) vs. 9.6 (4.5–12.7) months, $p<0.001$], 6-month (91.7% vs. 74.1%, $p<0.001$), and 1-year (58.3% vs. 3.7%, $p<.001$) survival rates were significantly increased compared with the stent group. KPS scores in the PDT+stent group were higher after 1, 3, and 6 postoperative months compared with the stent group ($p<0.05$). Incidence of postoperative adverse events was not significantly different (16.7% vs. 22.2%). Mean thickness of the tumor mass was significantly decreased after 1 and 3 postoperative months ($6.8\pm1.1$ vs. $13.8\pm4.1$ mm, $p=0.02$; $10.5\pm2.4$ vs. $15.4\pm3.9$ mm, $p=0.04$) and TNF-$\alpha$ and IL-6 levels were significantly increased 1 week postoperatively in the PDT+stent group compared with the stent group ($p<0.05$). TNF-$\alpha$ and IL-6 levels were significantly higher in the PDT+stent group compared with the stent group.
**Conclusion:** PDT combined with stent placement is an effective, safe treatment for EHCC can significantly improve alleviation of jaundice, prolong survival time, and improve quality of life, while not increasing the incidence of adverse events. The optimal time interval between PDT is 4 to 6 months. PDT could cause systemic inflammation in patients with EHCC in addition to direct destructive effect on cancer tissue.
**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1173 PREOPERATIVE ENDOSCOPIC BILIARY DRAINAGE PROCEDURES MAY AFFECT INTRAHEPATIC RECURRENCE OF CHOLANGIOCARCINOMA AFTER SURGICAL RESECTION


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**Introduction:** The best available potential curative therapy for cholangiocarcinoma is complete surgical resection. Peroperative biliary decompression is frequently performed in clinical setting.
**Aims & Methods:** To determine the impact of preoperative endosopic nasal biliary drainage (ENBD) and/or endoscopic retrograde biliary drainage (ERBD) procedures on intrahepatic recurrence rate in patients with cholangiocarcinoma after surgical resection, we performed this study. Between January 2005 and January 2015, 126 patients diagnosed cholangiocarcinoma and received surgical resection were included. Among 126 patients, 85 patients were treated with preoperative ENBD and/or ERBD. We retrospectively analysed prognostic factors (age, gender, preoperative ENBD and/or ERBD, tumor differentiation, pT factor, lymph node metastasis, surgical margin, lymphovascular invasion, preoperative maximal total bilitubin, postoperative chemoradiation/chemotherapy/radiation therapy, CA19–9) for recurrence after surgical resection.
**Results:** Intrahepatic recurrence after surgical resection was detected in 23/85 (27%) patients with preoperative ENBD and/or ERBD, and 4/41(9.7%) patients without preoperative ENBD and/or ERBD for median period of 12.5 months (range 0–115). The overall 1-, 3-, and 5-year cumulative recurrence rates were 24.6%, 36.9% and 36.9%, with preoperative ENBD and/or ERBD, and were 6.2%, 11.4% and 20.3%, without preoperative ENBD and/or ERBD, respectively ($P = 0.032$). On univariate analysis, intrahepatic recurrence rate of patients who underwent ENBD and/or ERBD ($n = 85$) was higher than that of patients who did not ($n = 41$) ($P = 0.042$) and that of patients who had elevated CA19–9 ($> 200$) ($n = 43$) was higher than that of patients who had not ($n = 83$) ($P = 0.001$). In multivariate analyses, preoperatively ENBD and/or ERBD and elevated serum CA19–9 level ($> 200$ ng/mL) were prognostic factors for intrahepatic recurrence, with hazard ratios (HR) of 3.203, (95% confidence interval (CI) 1.098–9.347, $P = 0.033$) and 3.930 (95% CI 1.803–8.569, $P = 0.001$), respectively.
**Conclusion:** Preoperative ENBD and/or ERBD procedures may affect intrahepatic recurrence of tumor in patients with cholangiocarcinoma after surgical resection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1174 CONTRAST-ENHANCED ULTRASONOGRAPHY OF GALLBLADDER POLYPOID LESIONS

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**Introduction:** To determine whether contrast-enhanced ultrasonography with perflubutane (Sonazoid®; Daiichi-Sankyo, Tokyo, Japan) can differentially diagnose gallbladder polypoid lesions.
**Aims & Methods:** We treated 179 patients with polypoid lesions of the gallbladder including adenocarcinoma ($n = 10$), adenoma ($n = 3$), benign polyps ($n = 138$), and fundal adenomyomatosis ($n = 28$). Lesions were assessed by ultrasonography using an Aplio 500 TUS-A500 (Toshiba Medical Systems, Tokyo, Japan) and a Prosound alpha10 (Hitachi Aloka Medica Ltd., Tokyo, Japan). The largest cross-section of lesions was initially visualized using B-mode ultrasonography with an infusion of Sonazoid®. The characteristics and behavior of blood flow in lesions during the early vascular phase were assessed over a period of about 30 sec and then observed for approximately the next 3 min. Thereafter, lesions were assessed using contrast harmonic and real-time perfusion imaging with infused Sonazoid®. Microflow imaging and capture mode proceeded after replenishing the Sonazoid®. The regions of interest were configured for all lesions and time intensity curves (TIC) of brightness were analyzed.
**Results:** Gallbladder cancer was characterized by hypervascular staining and the "eruption sign" that resembles vigorously boiling water splashing from the entire lesion in 11 (78.5%) of 14 patients. Blood flow images revealed irregularly sized, buckled and tortuous vessels as well as erratic blood flow in 8 (57.1%) of these patients. Gallbladder adenoma was also characterized by the eruption sign in 2 (66.7%) of 3 patients. Staining was scattered among gallbladder benign polyps and the "flicker sign" resembling bubbling already boiled hot water was evident in 130 (94.2%) of 138 patients. Staining was hypervascular in a few patients. Contrast enhancement was less persistent in gallbladder benign polyps than in cancer. Blood flow images revealed normal vessels. Staining of gallbladder fundal adenomyomatosis was scattered and mild flicker signs were evident in 26 (92.9%) of 28 patients. Blood flow was obvious at the surface of the prominence and at the internal Rokitansky-Aschoff sinus.Regions of interest were configured for all lesions and analysis of TIC for gallbladder cancer revealed a tendency towards sustained, intense brightness.
**Conclusion:** Contrast-enhanced ultrasonography using Sonazoid® can detect hemodynamics and differentially diagnose gallbladder polypoid lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1175 FACTORS ASSOCIATED WITH TECHNICAL SUCCESS OF BILATERAL ENDOSCOPIC METALLIC STENTING WITH PARTIAL STENT-IN-STENT PLACEMENT IN PATIENTS WITH MALIGNANT HILAR BILIARY OBSTRUCTION

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**Introduction:** It is controversial whether unilateral or bilateral self-expandable metallic stent (SEMS) placement is preferable in patients with malignant hilar biliary obstruction. Bilateral biliary drainage decreases the risk of cholangitis, but bilateral endoscopic metallic stenting is technically challenging.
**Aims & Methods:** We retrospectively evaluated factors associated with successful bilateral SEMS placement with the partial stent-in-stent (PSIS) method for malignant hilar biliary obstruction and the safety and efficacy of this technique. From April 2010 to February 2016, 47 consecutive patients (mean age, $73.0 \pm 8.8$ years; 32 males and 15 females) were treated with PSIS placement for malignant hilar biliary obstruction in our hospital. Patients were excluded from this study if they were previously treated with SEMS placement, underwent side-by-side placement, or had prior gastric surgery with gastrointestinal reconstruction. The technical success rate for PSIS, clinical response, and complications were investigated. Factors associated with technical success of PSIS were assessed. In patients treated with bilateral SEMS placement, procedure time, clinical response, and complications were compared based on whether the size of the SEMS delivery system was less than 6.0 Fr. Clinical response was defined as a serum total bilirubin decline to a normal level ($< 1.2$ mg/dL) or less than half of the pre-SEMS placement level.
**Results:** The technical success rate was 77%. Successful biliary decompression was achieved in 92% of patients. The clinical response rate was 91% and the complication rate was 26%. Regarding complications, pancreatitis occurred in five patients (11%), cholangitis occurred in six patients (13%), and cholecystitis occurred in one patient (2%). Multiple logistic regression analysis identified the use of a SEMS with a delivery system less than 6.0 Fr as a factor associated with technical success ($P = 0.046$; odds ratio, 0.112; 95% confidence interval, 0.013–0.966). In patients who underwent bilateral endoscopic metallic stenting, procedure time (ERCP time plus stenting time) was significantly shorter in patients with delivery system size $< 6.0$ Fr ($P < 0.01$). There were no significant differences in the clinical response or complication rate between the two groups.
**Conclusion:** Use of a delivery system with size less than 6.0 Fr contributes to an improved technical success rate and shortens the procedure time.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1176 ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE FOR BENIGN BILIARY STRICTURE AND PREOPERATIVE BILIARY DRAINAGE

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**Introduction:** Many studies have reported the effectiveness of endoscopic ultrasound-guided biliary drainage (EUS-BD) for palliative treatment of biliary strictures caused by unresectable malignancies. We often experience biliary strictures which are unable to achieve transpapillary biliary drainage, also with benign diseases or preoperative malignancies. However, the utility of EUS-BD for such cases was controversial.
**Aims & Methods:** The aim of this study was to clarify the acceptability of EUS-BD against benign diseases and preoperative malignancies. We reviewed 54 consecutive patients (35 males; mean age, 70.7 years) treated with EUS-BD from October 2008 to December 2015. A total of 57 EUS-BDs, 30 EUS-guided choledochoduodenostomies (EUS-CDS), 23 EUS-guided hepaticogastrostomy (EUS-HGS) and 4 EUS-guided randez-vous were performed, and we devided them into 3 groups as described; group A: benign biliary strictures (7 cases), group B: preoperative biliary drainages (11 cases), and group C: unresectable malignancies (39 cases). We evaluated the clinical outcomes of group A and B, compared to group C.
**Results:** Technical successes were achieved in 6 cases (85.7%) in group A, 10 cases (90.9%) in group B, and 32 cases (78.0%) in group C. Among them, 5 cases (83.3%), 9 cases (90.0%), and 29 cases (90.6%) were clinically effective, respectively. Early complications occurred in 1 case each in group A and B (1 peritonitis each), while there were 17 cases in group C (6 peritonitis, 3 double puncture, 3 cholangitis, 2 bleeding, 2 pancreatitis, and 1 dislocation). Late

complications occurred in 1 case in group B (dislocation), and 2 cases in group C (1 dislocation and 1 relapse cholangitis). Although clinical efficacy was not obtained in a case of severe pancreatitis with cholangitis in group A, other cases achieved long-term patency, and only 1 case required re-intervention to date. In group B, 2 cases underwent unscheduled surgical resection due to stent dislocation, among the 9 cases which ended up operable. Six cases successfully maintained their drainage route, but 3 cases of them required re-intervention before surgery. There were no dissemination and surgical failure due to EUS-BD procedure.
**Conclusion:** In this study, EUS-BD was effective for benign biliary stricture and preoperative biliary drainage in large, except for severe infection. For a reliable evidence of the utility of EUS-BD against benign biliary strictures, further reviews with long-term outcomes would be required.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1177 STENT PATENCY IN ENDOSCOPIC ULTRASOUND GUIDED TRANSMURAL VERSUS TRANSPAPILLARY BILIARY DRAINAGE


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**Introduction:** Endoscopic ultrasonography guided biliary drainage (EUS-BD) is an effective alternative to failed endoscopic retrograde cholangiopancreatography (ERCP). EUS-BD is performed either by transmural (EUS-choledocoduodenostomy or EUS-hepatogastrostomy; EUS-BD-TM) or transpapillary (antegrade or rendezvous; EUS-BD-TP) techniques. Data regarding efficacy of these modalities is limited.
**Aims & Methods:** Aim: To compare stent patency after EUS-BD when performed via TM or TP approach using metal stents in inoperable malignant biliary obstruction (MBO). Methods: Retrospective data of patients undergoing EUS-BD using metal stents for palliation of unresectable MBO after failed ERCP from 2011 to 2015 was collected. Data included etiology and stage of disease, relevant clinical, laboratory and imaging findings, reason for failed ERCP, EUS-BD technique (TM or TP). Follow up (physical or telephonic) was obtained untill reappearance of jaundice, re-intervention or death. Statistical analysis included Kaplan-Meier graph and Log-rank test. $P < 0.05$ was considered significant.
**Results:** Total ERCPs during the study period at our centre = 4064; total EUS-BD = 108(2.6%); EUS-BD with metal stents for MBO = 71; follow up data was available for 56. EUS-BD-TP = 23 & EUS-BD-TM = 33. Both groups were comparable for demographic and clinical characteristics. Overall median stent patency for both groups was 77 days (IQR 48–228 days); & was similar in both groups, median 69 days (IQR 51 – 240) for TM and 87 days (IQR 42 – 213) for TP ($P = 0.35$). Stent related AE occured more in the TP group than in TM group (8– TP vs 4 – TM), although the difference was statistically not significant ($P = 0.08$). AE included stent migration (0 – TP vs 2 – TM) and cholangitis or stent occlusion (8 – TP vs 2 – TM).
**Conclusion:** Outcomes of EUS-BD by TM or TP approach are comparable in terms of stent patency.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1178 CLINICOPATHOLOGIC STUDY OF BILIARY INTRAEPITHELIAL NEOPLASIA IN CHOLANGIOCARCINOMA


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**Introduction:** Biliary intraepithelial neoplasia (BilIN), is well known as a precursor to cholangiocarcinoma (CC). However, how often BilIN occurs and what its clinical implications is largely unknown.
**Aims & Methods:** We aimed to study about the prevalence and characteristics of BilIN. We performed a retrospective study of patients with histologically confirmed CC in Korea University Guro hospital between Jan 2012 and December 2014. Gallbladder cancer, ampullary cancer and combined hepatocellular-cholangiocarcinoma were excluded. In this study, we analyzed the surgically resected specimens of 48 patients who underwent curative resection. Immunohistochemical analysis of MUC2, MUC5AC Ki-67, P53 and SMAD were also examined.
**Results:** Of enrolled 48 patients, 34 patients were extrahepatic CC and 14 were intrahepatic CC. Six patients had invasive carcinoma arising from intraductal papillary neoplasm (IPN). BilIN was found in 58% (28/48) and more frequently in extrahepatic CC, 74% than intrahepatic CC, 21%. In extrahepatic CC, size and gross type of tumor was not different according to BilIN status, but poorly differentiation was less in BilIN positive CC. BilIN1 was 1 case, BilIN2 was 7 cases, and BilIN3 was 20 cases. BilIN was found in 88% of patients with Ki-67 labeling index over 10%, in 65% of patients with p53 overexpression over 5%, and in 71% of patients with loss of SMAD expression. Expression of MUC5AC was observed in 65%, while MUC2 was negative in all patients.
**Conclusion:** BilIN is frequently found in extrahepatic CC. Tumor differentiation and progression was more favorable in BilIN-positive CC than BilIN-negative. Ki-67 is suggested to be related with the malignant transformation of BilIN in carcinogenesis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1179 CLINICAL OUTCOME OF STENT-IN-STENT METHOD IN BILATERAL SELF-EXPANDABLE METALLIC STENT DEPLOYMENT FOR MALIGNANT HILAR BILIARY OBSTRUCTION: TWO-CENTER RETROSPECTIVE STUDY


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**Introduction:** Endoscopists deploy bilateral self-expandable metallic stent (SEMS) in patients with malignant hilar biliary obstruction by stent-in-stent (SIS) or side-by-side (SBS) method. Especially, recent technical improvements have allowed common use of SIS despite difficulty in deployment. However, previous studies of SIS method showed the diverse duration of stent patency. We investigated that recent data of patency using SIS in bilateral SEMS deployment in patients with malignant hilar biliary obstruction.
**Aims & Methods:** We retrospectively reviewed the patient data in two tertiary hospital, South Korea. We analyzed the clinical outcomes including patent duration and overall survival in patients with malignant hilar biliary obstruction. Multivariate anaysis was performed to find the prognostic factor related with stent patency and overall survival.
**Results:** In total, 70 patients with malignant hilar biliary obstruction underwent SIS deployment in this study between 2011 and 2015. Median age was 67 years old and median follow-up duration was 126 days. The Bismuth classification was as follows: type II, 13 (18.6%); type III, 17 (24.3%); type IV, 40 (57.1%). There were 35 (50.0%) stent occlusion events during follow-up period. Complications related with biliary stent insertion occurred in 17 (22.4%) patients. The median stent patency and survival were 108 and 189 days, respectively. On multivariate analysis, early complication and baseline bilirubin level were independent prognostic factors related to stent patency (HR 3.105, 95% CI 1.125–8.571, $P = 0.029$; HR 2.431, 95% CI 1.123–5.186, $P = 0.024$). High-grade hilar biliary obstruction was a significant risk factor for stent patency.

| Variables | Values |
|---|---|
| Gender (male/female) | 38/32 |
| Age, years | 68.0 ± 12.3 |
| Diagnosis | |
| Cholangiocarcinoma | 37 (52.9%) |
| Gallbladder cancer | 22 (31.4%) |
| Others | 11 (15.7%) |
| Bismuth classification | |
| II | 13 (18.6%) |
| III | 17 (24.3%) |
| IV | 40 (57.1%) |
| Previous stenting | |
| Plastic | 25 (35.7%) |
| Metal | 2 (2.9%) |
| Baseline total bilirubin | 6.1 ± 11.1 |
| Baseline ALP | 450.0 ± 354.8 |
| Treatment | |
| Yes | 38 (56.4%) |
| No | 32 (43.6%) |

**Conclusion:** The stent patency of SIS method in bilateral SEMS insertion was low compared to previous results. We need further study and alternative option for patients with high-grade malignant hilar biliary obstruction.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**PANCREAS III – POSTER EXHIBITION**

### P1180 EVIDENCE OF HGF DEPENDED BONE MARROW DERIVED STEM CELLS MOBILIZATION IN ACUTE PANCREATITIS – A POTENTIAL LINK WITH REGENERATION?


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**Introduction:** Various studies indicate potential involvement of various populations of bone marrow derived stem cells (BMSCs) in the process of tissue regneration. Phenomen of BMSCs mobilization to the peripherial blood was recently described, inter alia, in patients with stroke, heart infarction, Crohn's disease and pancreatic cancer [1].Moreover, studies on animal models show involvment of BMSCs in the process of pancreatic regeneration [2,3].However, the precise mechanisms of BMSCs mobilisation to peripherial blood and tissues and their role in pathogenesis of pancreatic disorders in humans is still a subject of reasearch.
**Aims & Methods:** Comprehensive analysis of circulating populations of BMSCs: mesenchymal, hematopoietic, endothelial progenitor cells (MSCs, HSCs, EPCs, respectively) as well as population of very small embryonic like stem cells (VSELs) in patients with acute and chronic pancreatitis in relation to controls, clinical setting and selected chemoattractants for stem cells. 35 patients; 18 with acute (AP), 17 with chronic pancreatitis (CP), and 31 healthy controls were included to the study. The absolute numbers and the percentage of 10 populations of BMSCs: HSCs (CD45+/Lin-/CD133+, CD45+/Lin-/CD34+), MSCs (CD45-/Stro-1+/CD105+, CD45-/Stro-1 -/CD105+, CD45-/Stro-1+/CD105-, CD45-/CD90+/CD29+), EPCs (CD45-/CD31+/ CD133+, CD45-/CD31+/CD34+/KDR+,) and small CD45-/CD31-/CD133+, CD45-/Lin-/CD34+ cells that correspond to VSELs, were enumerated and counted in peripheral blood with flow cytometry (FACS). The serum concentrations of chemoattractive factors (stromal derived factor 1-$\alpha$, sphingosine-1-phosphate, complement proteins, hepatocyte growth factor) were measured by ELISA.
**Results:** A significant mobilization of circulating VSELs (Lin-CD45-CD34+) in patients with AP comparing to controls was observed ($p = 0.012$). This phenomenon strongly correlates with high concentrations of HGF ($p = 0.008$). The decrease of circulating other stem cells as HSCs,(Lin-CD45+CD133+) subpopulation and MSCs, both CD45-STRO-1+CD105- and CD45-CD90+CD29+ subpopulations in AP patients was noted ($p = 0.022$, $p = 0.040$, $p = 0.026$). In contract, in patients with CP only decrease of HSCs (Lin-CD45+CD133+)($p = 0.011$) and EPCs (CD45-CD31+CD34+)($p = 0.004$) was observed.
**Conclusion:** The results suggest that VSELs could play a role in the regeneration of pancreatic tissue in acute pancreatitis with HGF as a chemoattractive factor. The mobilization of BMSCs to the peripheral blood, in pancreatic inflammatory disorders seems to be associated only with acute pancreatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1181 PROTECTIVE EFFECT OF CHEMERIN IN ACUTE PANCREATITIS. STUDY ON THE RAT


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**Introduction:** Chemerin is an immunomodulatory protein secreted mainly by adipocytes and skin cells. This adipokine stimulates chemotaxis of macrophages and NK cells toward the site of inflammation, but on the other hand, chemerin has been shown to reduce synthesis of pro-inflammatory cytokines. Chemerin signal was detected in the pancreas and this adipokine is involved in the insulin secretion, but the role of chemerin in the pancreatic inflammation is unknown.
**Aims & Methods:** To determine the effects of chemerin on caerulein-induced pancreatitis (AP) in the rats and on the nuclear factor kB (NF-kB) and tumor necrosis factor alpha (TNFalpha) protein signals in AR42J pancreatic acinar cell line. AP was induced by subcutaneous caerulein infusion (25 microgr/kg). Chemerin (1, 5, or 10microgr/kg was given intraperitoneally to the rats 30 min prior to the induction of AP. Blood samples were taken for evaluation of amylase and TNFalpha concentrations. Protein signals of NF-kB and TNFalpha were determined by Western blotting in AR42J pancreatic cells subjected to chemerin ($10^{-12}$, $10^{-10}$, $10^{-8}$ M) without or with addition of caerulein ($10^{-8}$ M).
**Results:** AP was confirmed by histological examination and by the increases of amylase and TNF alpha blood levels (by 600% and 300%, respectively). Chemerin markedly diminished histological manifestations of AP and decreased amylase and TNFalpha blood levels. In AR42J cells chemerin decreased protein signals for NF-kB p65 and TNFalpha induced by caerulein ($10^{-8}$ M).
**Conclusion:** Chemerin attenuated acute pancreatitis and this effect could be related, at least in part, to the reduction of proinflammatory pathway in pancreatic acinar cells.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1182 DEVELOPMENT OF ACUTE PANCREATITIS PORCINE MODEL BY USING ENDOSCOPIC RETROGRADE NOXIOUS AGENT INFUSION


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**Introduction:** Acute pancreatitis is an inflammatory disorder that affects the pancreas and surrounding organ. About 85% to 80% of acute pancreatitis patients show a benign clinical course, which is relatively easy to cure and responds well to conservative treatment. Meanwhile, the other 15% to 20% of patients develop a severe hemorrhagic necrotizing pancreatitis, follows a grave clinical course that is more often accompanied by multi-organ failure despite intensive careful treatment or surgery. However, effective specific treatment strategies are limited due to a poor understanding of its exact pathogenesis. A better understanding of the pathogenesis of acute pancreatitis may lead to more effective therapeutic options, potentially leading to improved survival. However, access to the pancreas during the different stages of acute pancreatitis is very limited because of the anatomical location of pancreas.
**Aims & Methods:** The aim of this study was to develop an animal model of acute pancreatitis using endoscopic methods. This experimental study was conducted on 6 mini pigs. Pancreatitis models were induced by pressure-controlled (1.000 or 100 mmHg) infusion of contrast media or sodium taurocholate (TCA) into the main pancreatic duct using endoscopic retrograde pancreatography. The animals were randomly allocated into three groups: (1) contrast-induced pancreatitis (2) 10% TCA-induced pancreatitis, (3) 20% TCA-induced pancreatitis. Injury of the pancreas was evaluated histologically. Serum amylase and lipase level were measured.
**Results:** Endoscopic procedures were performed successfully in all animals. No technical difficulty or adverse events occurred during the procedures. Acute pancreatitis in all animals was observed on hematologic and histologic examination. There was a significant increases in serum amylase and lipase levels (>10 times of baseline level) and they observed increases in pancreatic edema formation, vacuolization of acinar cell, and hemorrhagic necrosis. Degree of pancreatitis in the TCA (the mean histologic acute pancreatitis score, 10) groups tended to be greater than contrast-induced group (6.5). An analysis of degrees of pancreatitis according to concentration of TCA showed that the

higher concentration of TCA, the more severe pancreatitis was occurred (necrosis score in 20% TCA vs. 10% TCA, 4 vs. 2.5)
**Conclusion:** The two endoscopic procedures described are effective and safe for creating a swine model of acute pancreatitis. We estimated that these endoscopic methods could be helpful for developing the treatment strategy of acute pancreatitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1183 ACENOCOUMAROL ACCELERATES RECOVERY IN ISCHEMIA/REPERFUSION-INDUCED ACUTE PANCREATITIS

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**Introduction:** Coagulation is one of the mechanisms of hemostasis. Its activation causes the clot formation to prevent blood loss from a damaged vessel. Coagulation disorders may take the form of insufficient or excessive clotting. Insufficient clotting can result in bleeding or hemorrhage; whereas excessive activation of clotting can lead to thrombosis and/or disseminated intravascular coagulation (DIC). Moreover, there is close bidirectional relationship between coagulation and inflammation. Activation of the coagulation induces inflammation, but at the same time the development of the inflammatory process activates the clotting cascade. Previous studies have also shown that coagulative disorders occur in acute pancreatitis and are related to the severity of this disease.
**Aims & Methods:** Aim of the present study was to examine whether administration of acenocoumarol affects the course of ischemia/reperfusion-induced acute pancreatitis. Materials & Methods: Acute pancreatitis was induced in anesthetized rats by pancreatic ischemia followed by reperfusion. Saline or acenocoumarol at the dose of 50, 100 or 150 $\mu$g/kg/dose were administered intragastrically once a day, starting the first dose 24 h after the initiation of pancreatic reperfusion.
**Results:** Morphological features of pancreases showed that treatment with acenocoumarol reduces pancreatic edema, necrosis, and hemorrhages. Also, a decrease in pancreatic inflammatory infiltration and vacuolization of pancreatic acinar cells was observed in rats treated with acenocoumarol. These findings were accompanied with a reduction in serum activity of lipase and amylase, serum concentration of interleukin-1$\beta$ and plasma D-dimer concentration. Moreover administration of acenocoumarol improved pancreatic blood flow and pancreatic DNA synthesis. Acenocoumarol given at the dose of 150 $\mu$g/kg/dose was the most effective in the treatment of early phase of acute pancreatitis; however later, acenocoumarol given at the highest dose failed to exhibit any therapeutic effect; whereas lower doses of acenocoumarol were still effective in the treatment of acute pancreatitis.
**Conclusion:** Administration of low doses of acenocoumarol after the development of acute pancreatitis accelerates recovery in this disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1184 PROTECTIVE MECHANISMS OF N-ACETYL-CYSTEINE AND SIMVASTATIN AGAINST CHRONIC PANCREATITIS: AN EXPERIMENTAL STUDY IN MICE

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**Introduction:** Although anti-oxidants and anti-fibrotic agents could act as therapeutics in chronic inflammation, its effect is still unclear in chronic pancreatitis (CP). In our previous study, we investigated that simvastatin as anti-fibrotic agent was effective to modurate of cell proliferation in pancreatic stellate cells.[1] However, its effect and mechanism in CP was not proven in vivo. And developing an appropriate animal model of CP is also challenging.
**Aims & Methods:** In this study, we compared animal models of CP and investigated the therapeutic effect of N-acetyl-cysteine (NAC), an antioxidant, and simvastatin, an anti-fibrotic agent, on CP. Animal models of CP were generated by repeated intraperitoneal injection of cerulein (50 ug/kg) in BALB/c and C57BL/6 mice, hourly for 6 hours, thrice a week, for 4 or 8 weeks. Pancreatic weights, pancreas/body weight ratios, and histopathologic findings were compared. Using the best animal model, we evaluated the therapeutic effect of NAC and simvastatin alone or in combination on CP by assessing pancreas/body weight ratios, histopathologic findings (H&E and Sirius red staining), and western blot analysis [$\alpha$-SMA, collagen type I, and extracellular signal related kinase (ERK) 1/2].
**Results:** The pancreatic weight was significantly lower in C57BL/6 than in BALB/c mice with CP. Atrophic changes appeared earlier in C57BL/6 mice, their pancreas/body weight ratio was significantly different after 4 weeks of treatment. The pancreas/body weight ratio was about 1% in the control C57BL/6 mice and about 0.6% in mice with CP. In this experimental CP model using C57BL/6 mice, NAC and NAC + simvastatin combination therapy effectively prevented pancreatic atrophy (NAC group, 0.78%; NAC + simvastatin group, 0.82%). Acinar cell atrophy was alleviated by administration of NAC and/or simvastatin. Additionally, the fibrosis area was significantly reduced by NAC and/or simvastatin treatment. While cerulein administered mice showed a 5.6 fold increase in the pancreatic fibrosis area when compared to that of control mice, NAC and/or simvastatin treatment significantly decreased fibrotic changes against cerulein-induced pancreatic damage. ERK 1/2 and $\alpha$-SMA expressions were significantly decreased by NAC + simvastatin treatment, but not significant in collagen type I.
**Conclusion:** The C57BL/6 mouse is a better model of CP generated by intraperitoneal injection of cerulein (50 ug/kg), hourly for 6 hours, thrice a week, for 4 weeks. NAC and simvastatin alone or in combination have therapeutic effects against CP. And, the inhibition of ERK pathway would be one of the targets for treatment of CP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1185 INTESTINAL FATTY ACID BINDING PROTEIN AS A MARKER OF NECROSIS AND SEVERITY IN ACUTE PANCREATITIS

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**Introduction:** About 20% of acute pancreatitis (AP) cases are severe with considerable mortality rate of 10–25%. Despite several scoring systems and markers used, none are offering high sensitivity and specificity in identifying patients with a high risk of severe acute pancreatitis.
**Aims & Methods:** This study aimed to evaluate intestinal fatty acid binding protein (i-FABP) as potential marker for severity assessment and prediction of AP. The study was designed as part of the Pancreas 2000 educational program. Patients with AP were prospectively included at 5 clinical centers the years 2010–2012. Local complications were confirmed by performing abdominal CT. Severity of AP was determined based on 1992 Atlanta criteria[1] as data was collected before the revision of Atlanta classification. Serum i-FABP levels at day 1 and 3 of AP were determined using ELISA. Mann-Whitney U-test, Chi-square, Multivariate logistic regression analysis and ROC curve tests were used for statistical analysis.
**Results:** In the cohort of 402 patients (253 men, 149 women), 65 patients had severe AP. Serum i-FABP levels at day 1 were significantly higher in patients with pancreatic necrosis (median – 698 pg/mL vs 342 pg/mL), in patients having systemic complications (median – 501.5 pg/mL vs 382.5 pg/mL), in patients treated invasively (median – 549.5 pg/mL vs 379.5 pg/mL) in patients treated in ICU (median – 578 pg/mL vs 372 pg/mL) in patients with severe AP (median – 638.5 pg/mL vs 353 pg/mL) and in deceased patients (1073 pg/mL vs 382.5 pg/mL). i-FABP levels at day 1 yielded an AUC of 0.732 with an optimal cut-off value of 537 pg/mL in discriminating patients with pancreatic necrosis (sensitivity - 73.3%, specificity of 70.2%, negative predictive value (NPV) – 96.6%, positive predictive value (PPV) – 18.6%). Furthermore, i-FABP levels at day 1 of AP provided AUC of 0.669 with an optimal cut-off value of 465.5 pg/mL in predicting severe AP (sensitivity - 62.7%, specificity - 64.2%, NPV – 89.21%, PPV – 26.66%). Multivariate logistic regression analysis revealed that a model including i-FABP levels at day 1, lactate levels, CRP at day 2 was superior to either of these markers used alone in predicting severe AP – AUC of 0.874 (sensitivity - 41.6%, specificity - 96.64%, NPV – 85.1%, PPV – 78.26%).
**Conclusion:** Higher i-FABP levels on day 1 of AP were associated with pancreatic necrosis, systemic complications and severe AP. i-FABP levels on day 1 had a high negative predictive value for pancreatic necrosis and severe AP. Combination of several markers, including i-FABP, in predicting severe AP was superior to either of markers used alone.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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| | BISAP≤ 1 (n = 40) | BISAP≥ 2 (n = 35) | P Value | HAPS Positive (N = 40) | HAPS Negative (n = 35) | P Value |
|---|---|---|---|---|---|---|
| Mild Moderately Severe Severe | 36 4 0 | 7 17 11 | 0.0002 | 38 2 0 | 5 19 11 | 0.0001 |
| Age (years) | 35.3 ± 15.6 | 45.1 ± 19.4 | 0.01 | 41 ± 19.7 | 38.2 ± 16.2 | 0.49 |
| M/F | 33/7 | 28/7 | NS | 30/10 | 31/4 | NS |
| Duration of Hospital stay (days) | 4.8 ± 3 | 11.9 ± 10.2 | 0.0001 | 4.6 ± 2.9 | 12.1 ± 10.1 | 0.0001 |
| ICU stay (days) | 0.75 ± 1.2 | 5 ± 6.1 | 0.0001 | 0.8 ± 1.2 | 5 ± 6.1 | 0.0001 |
| Organ failure Transient Persistent | 0 0 | 5 11 | 0.0001 | 2 0 | 3 11 | 0.0004 |
| Infection Pancreatic Extrapancreatic Both | 0 0 0 | 3 3 5 | 0.0001 | 0 0 1 | 3 3 4 | 0.0021 |
| Mortality | 0 | 3 | 0.09 | 0 | 3 | 0.0021 |
| Need for intervention | 2 | 7 | 0.07 | 1 | 8 | 0.01 |

## P1186 COMPARING HAPS AND BISAP SCORES IN PREDICTING SEVERITY AND OUTCOME IN ACUTE PANCREATITIS

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**Introduction:** The Bedside Index for Severity in Acute Pancreatitis (BISAP) and Harmless Acute Pancreatitis Score (HAPS) have been shown to be useful for predicting the severity of acute pancreatitis. BISAP score comprises Blood urea nitrogen >25 mg / dl, Impaired mental status, Systemic inflammatory response syndrome (SIRS), Age > 60 years, and Pleural effusion. HAPS is considered positive when there is no rebound tenderness, normal hematocrit and a normal creatinine.

**Aim**: The aim of this study was to compare the performance of BISAP with HAPS in predicting severity, mortality, length of hospital stay, ICU stay, organ failure, infections and need for interventions in patients with acute pancreatitis (AP).

**Methods**: Clinical and laboratory data from consecutive patients with AP admitted to our institution between June 2013 and July 2015 was retrospectively analyzed. The BISAP score and HAPS were calculated at admission. Patients were classified into mild, moderately severe or severe acute pancreatitis as per the Revised Atlanta classification.

**Results:** Seventy-five patients with AP were included in the study, with a mean age of 40.3 years (of which 81.3% were male). Forty-three patients (57.3%) had mild AP and 32 patients (42.7%) developed moderately severe or severe acute pancreatitis. Overall, 3 (4%) patients died, 11 patients (14.67%) developed infections and 16 patients (21.3%) developed organ failure. BISAP ≤ 1 and HAPS positive at admission accurately predicted a mild course of acute pancreatitis in 83.7% (AUROC 0.92, Accuracy 85.33%) and 88.3% (AUROC 0.95, accuracy 90.67%) of patients, respectively. The sensitivity, specificity, PPV and NPV of BISAP ≤ 1 for predicting a mild course was 83.7% (95% CI 69.3 to 93.1%), 87.5% (95% CI 71–96.5%), 90% (CI 76.3 to 97.2) and 80% (CI 63 to 91.5%) respectively. In comparison, HAPS had a PPV of 95% (95% CI 83 to 99.3%), NPV of 85.7% (95% CI 69.7 to 95.1%), sensitivity of 88.3% (95% CI 74.9 to 96.1%) and specificity of 93.7% (95% CI 79.1 to 99.2%). Patients with BISAP ≤ 1 or HAPS positive had a significantly shorter hospital and ICU stay, lower risk of infection and organ failure when compared to BISAP ≥ 2 or HAPS negative (Table 1). However they did not predict mortality. HAPS positive at admission had significantly fewer interventions.

**Conclusion:** HAPS and a BISAP are accurate for risk stratification in patients with acute pancreatitis and can be used for patient triage and predicting outcomes. HAPS positive and BISAP ≤ 1 at admission accurately predict a mild course of acute pancreatitis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1187 INFLUENCE OF FATTY LIVER ON THE CLINICAL OUTCOME IN ACUTE PANCREATITIS

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**Introduction:** Acute pancreatitis (AP) is a common disease in the departments of gastroenterology with the variable severity, from being mild and self-limited to severe and fatal. During the last decades, the rate of death has not significantly declined, in spite of development of modern medicine. Therefore, the early recognition of high-risk patients is of a great interest. The aim of our study was to investigate the relationship between the presence of fatty liver disease and the course of AP determined by disease severity, the presence of local and systemic complications and survival rate.

**Aims & Methods:** A total of 1028 patients with the diagnosis of AP were initially evaluated in the period from January 1, 2008 up to June 31, 2015. Of the 1028 included patients, 138 patients were excluded due to alcoholic etiology of AP. Of the remaining 890 patients with AP, 68 were excluded due to uncertain etiology of AP. A total of 822 patients with AP were included in the final analysis. The most common etiology of AP was biliary (83.7% of patients). The diagnosis and the severity of AP were made according to the revised Atlanta classification criteria from 2012. Fatty liver disease was assessed by multislice computed tomography (MSCT) and/or magnetic resonance cholangiopancreatography (MRCP). Therefore, nonalcoholic fatty liver disease (NAFLD) was diagnosed by the presence of following findings: steatosis was detected by imaging (MSCT and/or MRCP); alcoholic etiology of AP was excluded; patients with specific disease or therapy than can lead to steatosis were not a part of this analysis.

**Results:** Of 822 patients with AP, 198 fulfilled the criteria for NAFLD. There was no significant difference due to age, gender, presence of coronary heart disease, chronic kidney disease as well as due to etiology of AP (biliary, hypertrygliceridemia and other etiologies of AP) between the patients with NAFLD and those without fatty liver (FL). Patients with NAFLD had statistically significantly higher incidence of arterial hypertension (54.5% vs. 43.3%; p = 0.007), diabetes mellitus type 2 (22.7% vs. 9.6%; p < 0.001), dyslipidemia (22.2% vs.8.2%; p < 0.001), as well as higher values of body mass index (29.1 ± 4.6vs. 27.3 ± 4.6; p < 0.001) and waist circumference (105.4 ± 13.6vs. 100.1 ± 13.1; p = 0.0003). Patients with NAFLD had a higher values of APACHE II score at admission, as well as higher levels of C-reactive protein (CRP) at the admission, as well as higher levels of CRP at day three in comparison to the AP patients without FL. Additionally, NAFLD patients had higher incidence of local (0.9 ± 0.9 vs. 0.3 ± 0.7; p < 0.0001) and systemic (0.4 ± 0.8 vs. 0.2 ± 0.6; p = 0.002) complications, as well as higher values of CT severity index (2.9 ± 2.9 vs. 1.1 ± 2; p < 0.0001) in comparison to those without NAFLD. Patients with NAFLD had a statistically longer total hospital stay (15.4 ± 10.6 vs. 12.9 ± 8.2; p = 0.0006), higher dependency unit stay (4.5 ± 3.6 vs. 3 ± 3.2; p < 0.0001) and had a statistically longer stay in intensive care unit (1.0 ± 5.1 vs. 0.3 ± 1.9; p = 0.004) in comparison to the patients without FL. Comparing survival rates, AP patients suffering from NAFLD had a higher death rate compared to patients without NAFLD (5.6%vs. 4.3%; p = NS), although that difference was not statistically significant.

**Conclusion:** The presence of NAFLD at admission portends a higher risk of moderately severe and severe AP. Patients with NAFLD developed more local and systemic complications in AP. NAFLD patients also had higher mortality rate (although that was not statistically significant) and longer duration of hospital stay, as well as longer stay in intensive care unit. Therefore, the presence of fatty liver in patients admitted because of acute pancreatitis may play a prognostic role in these patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1189 FAT GLOBULES WITHIN ORGANIZED PANCREATIC FLUID COLLECTIONS ON CT SCAN IMPACT THE OUTCOMES OF NONSURGICAL DRAINAGE

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**Introduction:** T2-weighted MRI is the most accurate means of quantifying debris in organized pancreatic fluid collections (PFC) but is rarely obtainable over computed tomography (CT) prior to drainage. Debris within PFC represents necrosis of pancreatic fat and its presence can affect the approach to drainage.

**Aims & Methods:** To assess whether the presence of fat globules in PFCs on CT scan impacts the outcomes of non-surgical drainage. Patients with an organized PFC as well as CT scan obtained at least 4 weeks after their episode of acute pancreatitis between 1/1993 and 1/2015 were identified using an administrative database. CT scans were interpreted by single radiologist for the presence of fat globules defined as foci of fat attenuation. For those patients undergoing non-surgical drainage (endoscopic and/or percutaneous), differences in technical and clinical success in terms of completion of procedure, resolution in PFC size (<50% reduction) and need for reintervention (the need for a repeat procedure for the same PFCs) were assessed between the PFCs with or without fat globules. Analysis was conducted using Pearsons Chi Square test or Fisher's exact tests for categorical variables and student's t test for continuous data.

**Results:** There were 58 patients identified with a mean age of 53.76 ± 15.08 years and 35 (60.3%) males. There were 77 PFCs evaluated as 13 patients had more than one PFC. There were 22 (29%) PFCs that spontaneously resolved whereas 55 (61%) PFCs required drainage after a mean of 24.5 ± 44.7 days from the time of PFC diagnosis. Fat globules were seen in 35 (45%) PFCs on CT with 21 PFCs drained endoscopically, 5 drained using

both endoscopic and percutaneous approach and 2 drained percutaneously as compared to 42 (55%) PFCs with no fat on CT of which 12 were drained endoscopically, 14 were drained percutaneously and 1 was drained using both endoscopic and percutaneous drainage ($p = 0.03$). Technical success was achieved in all PFCs. Among the PFCs with fat globules, 12 were endoscopically drained using lumen-apposing metal stents (LAMS) and 8 using double pigtail plastic stents versus 6 and 4 in PFCs without fat globules, respectively ($p = 0.001$). There were 9 PFCs with fat globules that required reintervention as compared to 3 PFCs without fat ($p = 0.024$). PFCs containing fat globules resolved after a mean time of $57.30 \pm 46.81$ days as compared to PFCs without fat globules which resolved after $29 \pm 25.1$ days ($p = 0.003$)

**Conclusion:** PFCs containing fat globules on CT scan more commonly required LAMS, combined drainage modalities, multiple interventions, and had a significantly longer duration to resolution as compared to PFCs without fat globules. Fat globules seen within PFCs on CT scan helps endoscopists with pre-procedure planning, thereby avoiding requirement of MRI to differentiate PFCs into walled-off necrosis or pseudocyst.

**Disclosure of Interest:** M. Khashab: Consultant for Boston Scientific, Xlumena and Olympus

A.N. Kalloo: Equity holder for Apollo Endosurgery

V. Singh: Consultant for Abbvie, CalciMedica, and Novo Nordisk. Advisory board participant for Enteromedics, Celltrion, and Salix

All other authors have declared no conflicts of interest.

## P1190 THE ROLE OF SOLUBLE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR AS AN EARLY BIOMARKER OF SEVERITY AND ORGAN FAILURE IN PATIENTS WITH ACUTE PANCREATITIS

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**Introduction:** Acute pancreatitis (AP) is an inflammatory condition with a high mortality rate in the severe cases. Conventional biomarkers like C-reactive protein (CRP) fall short in their ability to predict severity in early-phase AP. We assessed suPAR, a soluble urokinase plasminogen activator receptor (suPAR), as an early prognostic biomarker in AP with respect to disease severity, organ failure and mortality.

**Aims & Methods:** During a 15-month period, 75 patients with their first episode of AP were prospectively enrolled in the study. Blood samples were drawn on day of admission, day 1, 2 and 14 and debut of symptoms were recorded. Data was collected from the medical records for age, gender, alcohol intake, smoking, medications, organ function and need for intensive care unit (ICU).

**Results: Results:** suPAR levels were significantly related to ICU ($p = 0.013$) and renal failure ($p = 0.021$) but we found no association to multi organ failure (MOF). There was a significant association between suPAR levels at admission and mortality ($p = 0.004$). A subgroup analysis of AP demonstrated a significant increase in suPAR over time in patients with other causes of AP than alcohol and gallstone (p=0.015). However, for all comers with AP, suPAR levels didn't change significantly over time.

**Conclusion:** Our results suggest, that although suPAR is associated with disease severity and organ failure, it has poor predictive potential in AP.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1191 A HUNGARIAN FAMILY WITH HEREDITARY PANCREATITIS AND THE P.L104P MUTATION IN THE HUMAN CATIONIC TRYPSINOGENE GENE

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**Introduction:** Mutations in the human cationic trypsinogen gene (PRSS1) are associated with hereditary chronic pancreatitis. The most frequent mutations (p.R122H, p.N29I and p.A16V) cause early activation of trypsinogen inside the pancreas. Family members carrying these mutations develop chronic pancreatitis usually in childhood. Inheritance of chronic pancreatitis in these families follows an autosomal dominant pattern with incomplete penetrance. A subset of rare mutations such as p.L104P seem to exert their effect by causing trypsinogen misfolding and endoplasmatic reticulum stress. However, whether misfolding-causing mutations casue hereditray pancreatitis or sporadic disease only has remained unclear.

**Aims & Methods:** Our aim was to establish the association between the PRSS1 p.L104P mutation and the development of hereditary chronic pancreatitis in a Hungarian family. Genetic testing was performed in all family members who signed informed consent. Peripheral blood or buccal swabs were collected and genomic DNA was isolated. Sanger sequencing was carried out in all exons of PRSS1, CTRC, SPINK1 and CPA1 genes and in exon 4,10 and 11 of the CFTR gene of the index patient. Sanger sequencing of exon 3 of the PRSS1 gene was carried out in all other family members. Diagnosis of chronic pancreatitis was based on abdominal CT scan, abdominal ultrasound, clinical signs and indirect functional tests.

**Results:** Three members of a Hungarian family with clinically documented idiopathic recurrent acute and chronic pancreatitis carried the rare p.L104P mutation in the PRSS1 gene. First episode of acute pancreatitis was documented over 18 years of age in all cases. The rarely diagnosed pancreatolithiasis was also found in all affected individuals. Four members of the family also carried the same mutation without acute or chronic pancreatitis, however 3 of them are under 18 years of age. Family members without the investigated mutation did not develop pancreatitis.

**Conclusion:** This is the first study showing clear association between the PRSS1 p.L104P mutation and clinically documented hereditary chronic pancreatitis with unusual features of later age of onset and pancreatolithiasis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1192 DIAGNOSIS OF AUTOIMMUNE PANCREATITIS USING ENDOSCOPIC ULTRASOUND GUIDED PANCREATIC CORE BIOPSY WITH PROCORE® NEEDLE

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**Introduction:** Endoscopic ultrasound-guided pancreatic core biopsy (EUS-PCB) has been performed to establish histologic diagnosis of pancreatic disease. Recently Procore® needle with reverse bevel design has become available for EUS-PCB.

**Aims & Methods:** The aim of this study was to evaluate the usefulness of EUS-PCB using Procore® needles for the diagnosis of AIP. From June 2012 and November 2015, a total of 62 patients (18 in a 19-gauge needle group and 44 in a 22-gauge needle group) who were suspected with AIP included.

**Results:** A sample adequate for diagnosis was obtained more in 54 of 62 patients (87.1%). 54 patients (type 1 $n = 46$, type 2 $n = 8$) were diagnosed with AIP. Pancreatic malignancies were excluded in 8 patients (12.9%) by EUS-PCB. Lymphoplamacytic infiltration, storiform fibrosis, and abundant IgG4-positve cells were shown in 53.7% ($n = 29$), 40.7% ($n = 22$), and 48.1% ($n = 26$). Obliterative phlebitis was shown only in 19-gauge group ($n = 4$, 7.4%). Granulocytic epithelial lesions were shown in 3 (37.5%) patients. The 19 gauge group showed significantly more histologic findings than 22-gauge group ($n = 14$, 82.4% vs. $n = 17$, 45.9%, $p = 0.01$). Overall sensitivity, specificity of histologic diagnosis of AIP were 57.4%, 100%. The sensitivity was significantly higher in

**P1194**

| | Type of Needle | Macroscopic Evaluation | Microscopic score |
|---|---|---|---|
| 1 | ECHOTIP PROCORE (20 G) | Fragmented. Presence of core | 9 |
| 2 | SPIROTOME TM | Non-fragmented core | 6 |
| 3 | FRANSEEN LUNG Biopsy Needle (18 G) | Fragmented. Presence of core | 10 |
| 4 | TROCAR NEEDLE (18 G) | Micro fragments | 1 |
| 5 | CHIBA Biopsy Needle (20 G) | Fragmented. Absence of core | 1 |
| 6 | TURNER Biopsy Needle (20 G) | Non-fragmented core | 0 |
| 7 | CHIBA Biopsy Needle (18 G) | Fragmented. Presence of core | 7 |
| 8 | TURNER Biopsy Needle (18 G) | Doubtful presence of core | 0 |
| 9 | ECHOTIP PROCORE (22 G) | Doubtful presence of core | 2 |

the 19-gauge group (82.4% vs. 46%, $p < 0.01$). No adverse events were developed after EUS-PCB.
**Conclusion:** EUS-PCB using Procore® needle is a useful for histologic diagnosis of AIP. Especially EUS-PCB with a 19-gauge needle may more valuable method for histologic diagnosis of AIP when the diagnosis of AIP is uncertain.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1193 CORRELATION BETWEEN THE DEGREE OF PANCREATIC FIBROSIS AND PANCREATIC SECRETION OF BICARBONATE IN PATIENTS WITH EARLY MORPHOLOGICAL CHANGES OF CHRONIC PANCREATITIS


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**Introduction:** Morphological changes of chronic pancreatitis (CP) are significantly associated with functional alterations of the gland at advanced stages of the disease. This morphological-functional correlation has been shown not to be so evident in patients with early CP. It is well known that pancreatic secretion of enzymes and bicarbonate decreases as the fibrosis degree of the glans increases in CP. We have previously shown that the degree of pancreatic fibrosis in CP can be quantified by endoscopic ultrasound elastography (EUS-E). Pancreatic secretion can be accurately evaluated by the endoscopic pancreatic function test (ePFT), which can be used for the early diagnosis of CP.
**Aims & Methods:** Aim of the present study was to evaluate the correlation between the degree of pancreatic fibrosis and pancreatic bicarbonate secretion in patients with early morphological changes of CP. Methods: A prospective, cross-sectional study was designed. Patients with clinical suspicion of CP and 3–4 EUS criteria of the disease were included. EUS-E was performed with the slim Pentax Echoendoscope (EG-3270UK) and the HITACHI-Ascendus ultrasound equipment. Elastographic strain ratio (SR) was evaluated as the mean SR at the head, body and tail of the pancreas (normal < 2.25). After that, 0.2$\mu$g/kg secretin was intravenously administered and bicarbonate concentration was measured in samples of duodenal juice collected after 15, 30 and 45 minutes (normal peak > 80 mEq/L). Data are shown as mean ± SD and percentages. Correlation between SR and bicarbonate peak was analysed by linear regression.
**Results:** 43 patients were included (mean age 39.9 years, range 18–66, 22 female). 30 patients (69.8%) had 3 EUS criteria of CP, and 13 (30.2%) 4 criteria. Peak bicarbonate concentration was 66.1 ± 27.7 mEq/L. 33 (76.7%) patients had an abnormally low bicarbonate secretion. Mean SR was 3.55 ± 1.01 and it was abnormally high in all patients. Correlation between SR and bicarbonate secretion was highly significant ($r = 0.768$; $p < 0.0001$).
**Conclusion:** There is a strong correlation between the degree of pancreatic fibrosis as evaluated by EUS-elastography and stimulated pancreatic secretion of bicarbonate. These results support the use of EUS-E for the early diagnosis of CP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1194 ACCURACY OF DIFFERENT NEEDLES TO OBTAIN HISTOLOGICAL SAMPLES FROM HEALTHY PANCREATIC TISSUE. A COMPARATIVE EXPERIMENTAL STUDY ON HEALTHY PIGS


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**Introduction:** The diagnosis of early chronic pancreatitis remains a clinical challenge, especially in the absence of methods for histologic confirmation. Histological diagnosis could be possible by endoscopic ultrasound (EUS)-guided fine needle biopsy (FNB), but appropriate needles to obtain core tissue samples from a slightly fibrotic pancreas are lacking
**Aims & Methods:** Aim of this study was to evaluate the accuracy of different biopsy needles to obtain core tissue samples from healthy pancreas. Our goal, based on the results of this study, is to design a new EUS needle in collaboration with specialized biomedical engineers.
**Methods:** Pilot, single-blind, comparative, animal study of histological evaluation of FNB samples from healthy pig pancreas. The pancreas of a 2-months aged pig, 22Kg weight, was manually exposed after laparotomy under general anesthesia. Pancreatic samples obtained with nine different needles (Cook-Medical, Limerik, Ireland) were evaluated. Three biopsies were taken from the pancreas with each needle (total of 27 biopsies). A macroscopic descriptive evaluation of the samples was performed. All samples were coded and placed in formalin for blind histological evaluation. Histological quality of samples was scored from 0 to 10 by an expert pathologist on pancreatic cyto-histology, being 0 the absence of sample and 10 a sample suitable for histological and immunohistochemical study. This study was approved by the Ethics Committee of the Veterinary Hospital Rof Codina of Lugo.
**Results:** The table shows the macroscopic and microscopic evaluation of each of the needles evaluated.
**Conclusion:** The echotip-Procore 20 G and the Franseen lung 18 G needles provide very good tissue samples from the healthy pig pancreas. Whether EUS-guided FNB with the echotip-Procore 20 G needle is appropriate for the histological diagnosis of early chronic pancreatitis deserves further clinical research studies.
**Disclosure of Interest:** J. Iglesias-García: International advisor Cook Medical
J.E. Domínguez-Muñoz: International advisor Cook International
All other authors have declared no conflicts of interest.

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1. The echotip-Procore 20G and the Franseen lung 18G needles provide very good tissue samples from the healthy pig pancreas. Whether EUS-guided FNB with the echotip-Procore 20G needle is appropriate for the histological diagnosis of early chronic pancreatitis deserves further clinical research studies.


### P1195 TREATMENT OF PANCREATIC STONES BY ESWL AND ENDOSCOPY-OUR EXPERIENCE OF 618 CASES IN 26 YEARS


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**Introduction:** We have experienced 618 cases of pancreatic stone in our hospital over a period of 26 years; 482 alcoholic (male 442, female 40), 77 idiopathic (male 32, female 45),16 hyperparathyroidism,12 hereditary pancreatitis,11

divisum, 7 autoimmune pancreatitis, 6 anomalous pancreatobiliary union, 4 juvenile pancreatitis, 2 post surgical operation and 1 post papilla EMR.
**Aims & Methods:** Usefulness and safety of the medical treatment and their long prognosis were evaluated. 577 cases were treated medically (symptomatic 535, asymptomatic 42). 90 were treated by endoscopy alone, 50 by ESWL alone, and 437 by ESWL and endoscopy. 36 without symptoms had no therapy, and 3 were primarilly treated surgically. 88 cases were treated via minor papilla. 125 cases were complicated with pseudocyts.
**Results:** Stone-free-rate was 75% (462/613), pain-free-rate was 98% (519/535), stone-relapse rate was 6.2% (27/460) and the operation rate after medical treatment was 2.5% (16/577). Endocrine and exocrine function improved in 29%, 30% respectively. Cancer occurred in 21 cases (3.5%) - pancreas 6, lung 6, larynx and pharynx 4, esophagus 1, colon 1, liver 1, kidney 1 and choledochus 1.
**Conclusion:** The medical treatment (ESWL + endoscopy) of pancreas stones is a usuful and safety method with stone-free-rate 75%, pain-free-rate 98%, stone-relapse rate 6.2% without major complications. Patient with pancreatic stone have high risks for pancreatic, lung, laryngo-pharyngeal and esophageal cancer. So careful examination after stone removal is necessary.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1196 PREVALENCE OF SARCOPENIA IN CHRONIC PANCREATITIS

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**Introduction:** Over the time in the chronic pancreatitis (CP) patients both endocrine and exocrine insufficiency may develop and lead to different metabolic alterations, malnutrition. Little is known about muscle depletion or sarcopenia and its impact on CP disease course. Sarcopenia might be as a hint to early pancreatic exocrine insufficiency in patients with no specific complaints or negative results of functional tests.
**Aims & Methods:** Aim of the study was to evaluate the prevalence of sarcopenia, analyzed by additional measures of computed tomography (CT) imaging scans, in CP patients, as well it influence on the course of disease. The study was multicenter retrospective cohort study with data inclusion for one year time period, year 2015. Body constitution were analyzed by additional measurements of CT examinations. ImageJ v1.49q standard program (National Institutes of Health) for CT image analysis was used. The third lumbar vertebra (L3) was selected as the standard landmark measurements, chosen these image-level axial cuts. Muscular, visceral, subcutaneous and intramuscular adipose tissue areas were measured. Values were normalized for height to get the lumbar skeletal muscle index in $cm^2/m^2$. Sarcopenia cut-off values were used: 52.4 $cm^2/m^2$ for men, 38.5 $cm^2/m^2$ for women. Data about pancreas morphological changes by CT imaging, BMI, endocrine and exocrine insufficiency status were collected, sarcopenia influence was evaluated.
**Results:** The study included 140 patients with mean age 48 years (range 30–82 years); 98 males, 42 females. Assessing by CT images (according to the Cambridge classification) patient's morphological changes of the pancreas - 41 patients were marked, 76 patients – moderate, 23 – mild. Mean skeletal muscle indexes were 44.08 $cm/m^2$ for men, 38.55 for women $cm/m^2$. Sarcopenia was found in patients with chronic pancreatitis in 69% (96 patients). In patients with normal BMI sarcopenia was in 81% (57 patients, $n = 70$), with underweight 70% (7 patients, $n = 10$), with overweight and adiposity 53% (24 patients, $n = 45$; 8 patients, $n = 15$) ($p = 0.02$). Sarcopenia was not found significantly more often in patients with marked changes in the CT exam according to Cambridge classification ($p = 0.06$). No significant differences of sarcopenia in patients with diabetes mellitus ($n = 28$), proven exocrine insufficiency with enzyme supplementing therapy ($n = 16$) were found.
**Conclusion:** Sarcopenia was found quite often (69%) in patients with CP. Even in patients with normal or higher BMI, muscles depletion still was observed (53 – 70%). Proven sarcopenia might be an additional indication for more intense approach with enzyme replacement therapy and nutritional support, also physical activity and exercises could give improvement for CP therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1197 COMPARISON BETWEEN ENDOSCOPIC AND SURGICAL DRAINAGE OF THE PANCREATIC DUCT IN CHRONIC PANCREATITIS

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**Introduction:** Treatment of recurrent chronic obstructive pancreatitis is pancreatic duct decompression with endoscopic drainage (endoscopic pancreatic stenting [EPS] with extracorporeal shockwave lithotripsy [ESWL]) or surgical drainage. Despite the recent popularization of endoscopic treatment, treatment or stent removal is difficult in many patients. We compared the efficacy, safety, and medical cost of endoscopic and surgical treatments.
**Aims & Methods:** We retrospectively compared the treatment course and medical cost of hospitalization between 41 patients who had undergone pancreatic stenting between 2006 and 2010 and could be followed up for 1 year or longer (EPS group) and 10 patients who had undergone surgery for poor control of pancreatitis between 2001 and 2005 and could be followed up for 1 year or longer (surgery group). The EPS group included 35 men and 6 women with a mean-± standard deviation age of 59 ± 14 years who had a stenosis at the pancreatic head. The causes of recurrent chronic pancreatitis (CP) were alcohol consumption in 35 patients, pancreas divisum in 3 patients, postoperative anastomotic stenosis in 1 patient, and idiopathic in 2 patients. The surgery group included 5 men and 5 women with a mean ± standard deviation age of 49 ± 16 years. The causes of recurrent CP were alcohol consumption in 8 patients, postoperative anastomotic stenosis in 1 patient, and idiopathic in 1 patient. The types of surgery were pylorus-preserving pancreaticoduodenectomy (PpPD) in 6 patients, distal pancreatectomy (DP) in 2, and the Beger procedure in 2.
**Results:** In the surgery group, the patients were younger ($P = 0.07$) and the ratio of women to men was higher ($P = 0.03$) compared to the EPS group. No intergroup differences were observed in causes, symptoms, disease duration, smoking history, or endocrine and exocrine functions. The technical success rate was 100% in both groups, and pain was improved in all of the patients in the two groups. The incidences of complications did not differ significantly, and the mortality rate was 0% in both groups. The stents could be removed in 25 (61%) and maintained in 16 (39%) of 41 patients with stent placement. The mean stent placement period in the patients in whom stent removal was possible was 516 days (93–1438 days), the mean frequency of stent replacement was 2.7 (0–9 times), and the frequency of concurrent ESWL was 1.6 times. The mean medical cost of hospitalization was 1,350,130 yen. The mean stent placement period in the patients with continuous stenting was 1396 days (436–2534 days), the mean frequency of stent replacement was 8.2 times (2–17 times), the mean frequency of concurrent ESWL was 3.2 times, and the mean medical cost of hospitalization was 3,357,080 yen. Significant differences were noted for all four items ($P = 0.02$, $P < 0.01$, $P = 0.04$, and $P < 0.01$, respectively). In the surgery group, none of the patients underwent reoperation. However, 2 patients were rehospitalized (1 for stomal ulcer and 1 for sub-ileus). The rehospitalization rate was significantly higher in the EPS group (78%) than in the surgery group (20%; $P < 0.01$). This was considered attributable to rehospitalization for stent replacement. The effect to improve endocrine and exocrine functions was not different between the two groups before and after treatment, and the current condition was maintained in 80% or more of the patients. For the entire EPS group, the mean hospitalization period was 18 days and the mean medical cost of hospitalization was 2,133,330 yen. For the entire surgery group, the mean hospitalization period was 23 days and the mean medical cost of hospitalization was 2,246,548 yen, with no significant differences between the two groups.
**Conclusion:** Although both endoscopic and surgical treatments achieved high symptom control and safety rates, hospitalization is required for stent replacement, which leads to poor cost-effectiveness, particularly in patients in whom stent removal is difficult. Hence, surgery should also be considered.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1198 DESIGNING OF A NOVEL STRATEGY FOR CANCER GENE THERAPY BY SELECTIVE DELIVERY OF ADENOVIRUS-BASED TOXIN

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**Introduction:** Aberrant activation of the Ras pathway exists in many human tumors, such as pancreatic (PC) (90%) and colorectalcancers (CRC) (40%). Ras mutations have been associated with increased tumorigenicity. However, development ofdirect and in direct inhibitors has not proved to be effective. We propose to exploits the hyperactive Ras pathway. Wepreviously reported that recombinant adenoviruses, carrying a pro-apoptotic gene (PUMA) under the regulation of Ras-responsive elements suppressed the growth of cancer cells harboring hyperactive Ras. Moreover, we had shown thatby replacing PUMA with more potent toxins, such as the bacterial MazF-MazE toxin-antitoxin regulated system, thepotency of this killing strategy was significantly improved (Shapira et al,2015). P53 is a classical tumor suppressor, it'smutated in many malignancies (PC 75%, and CRC 60%)
**Aims & Methods:** To establish a tight control dual system based on the Ras and p53 responsive elements. Adenoviral vectors carrying the toxin (PY4-MazF-mcherry) and the antitoxin (RGC-MazE-IRES-GFP) were designedunder the regulation of Ras responsive elements and p53 responsive elements, respectively. Those two constructswere cloned into a "first generation" ΔE1/ΔE3 human type-5 adenoviral-vector. Virus particles were produced, theirtiter was calculated by the End-Point Dilution Assay and their potency was tested in vitro. Cell death was measuredqualitatively by using the fluorescent microscopy and was quantified by the enzymatic MTT assay. SHP77;Rasmut/p53mut, H2030;Rasmut/p53wt, H1650;Raswt/p53wt and H1975;Raswt/p53mut-lung cancer cell lines were used as amodel system for testing the potency of the

adenoviruses-based system. Mia Paca2, Colo357, Panc1;Rasmut/p53mut, and BxPC3; Raswt/p53mut-PC cell lines were tested as well. Co-infection assays were performed on our modelsystem in different toxin-antitoxin ratios (2:1, 1:1 and 1:0.5)
**Results:** Massive cell death was induced in a dose-dependent manner; 70% with a titer of 7.5 MOI in cells with hyper-activatedRas, compared to 21% in cells with WT Ras. The cytotoxic effect of the toxin was qualitatively confirmed byfluorescence microscopy. Similar therapy in PC lines expressing mutated Ras showed 50% cell death in a dosedependentmanner with a titer of 15 MOI, compared to 18% in cells with WT Ras. Co-infection with MazF andMazE encoded viruses, using the optimal 1:0.5 ratio, showed decrease in the mortality of the mutated Ras cellsexpressing WT p53; 36% with a titer of 7.5 MOI. These results indicate that cells that expressed the toxin wereprotected by the anti-toxin expressed under the p53 responsive element
**Conclusion:** Outside the box cancer gene therapy by exploiting activate Ras and P53 pathways are effective in vitro.The low toxicity in WT Ras as well as WT p53 expressing cells allows selective and safe therapy of cancer cells
**Disclosure of Interest:** N. Arber: Consultation fee: Bio-view, Check-cap, Bayer Stock Shareholder: Micromedic, GI-View
All other authors have declared no conflicts of interest.

## P1199 GSK3B INHIBITOR DOWN-REGULATES PD-L1 IN KRAS-MUTANT PDAC THROUGH INHIBITING NF-KB

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**Introduction:** Pancreatic ductal adenocarcinoma (PDAC) is the sixth leading cause of cancer death in the world, with a 5-year survival rate of less than 5%. Recent reports suggested that overexpression of programmed cell death ligand 1 (PD-L1), known as a ligand for PD-1, showed poor prognosis in patients with pancreatic cancer due to the deterioration of anti-tumor immune responses. Although the use of anti-PD-1 antibody, nivolumab, showed promising effect on variable cancers, the effect of anti-PD-1 on PDAC has not been fully confirmed yet. Since the regulation of PD-L1 expression has not been clarified yet, we sort to elucidate the signaling pathways to express PD-L1, and hypothesized that downregulation of PD-L1 expression could be one of the therapeutic option for PDAC treated with anti-PD-1 therapy.
**Aims & Methods:** The aim of this study was to elucidate the upstream signaling pathway to express PD-L1 in PDAC. We used pancreatic cancer tissue array to evaluate PD-L1 protein expression in pancreatic cancer by immunohistochemistry (PA1001a, US Biomax, Rockville, MD, USA). To clarify the upstream signaling pathways regulating PD-L1 expression, we tested 96 inhibitors on Panc1 pancreatic cancer cells in regulation of PD-L1 expression (inhibitors were provided by Screening Committee of Anticancer Drugs supported by Grant-in-Aid for Scientific Research, Japan). 24 hrs after adding 10 microM of each inhibitor, we selected candidate inhibitors that were able to downregulate PD-L1 mRNA/protein expression as assessed by real-time qPCR analysis or western blotting. We also performed cell proliferation assay (Cell Counting Kit-8, Dojindo, Kumamoto, Japan) by using these candidate inhibitors on the proliferation of pancreatic cancer cells.
**Results:** Fourteen out of forty-five pancreatic cancer cases (31%) were positive for PD-L1 protein expression as assessed by immunohistochemistry. There were no differences in positive rate of PD-L1 over gender, age, or clinical stages. Six out of 96 protein kinase inhibitors showed decreased PD-L1 protein expression in Panc1 cells compared with non-treated control cells, which consisted of five signaling pathways (Table 1). GSK-3 inhibitor IX was confirmed to inhibit PD-L1 mRNA/protein expression. Cell proliferation was also assessed and GSK-3 inhibitor IX was significantly inhibited cell proliferation time dependent manner. We also detected decreased activation of NF-$\kappa$B by inhibiting GSK3 pathway, and TNF-induced PD-L1 mRNA expression was downregulated by using NF-$\kappa$B inhibitor, MG132 (20microM) (relative PD-L1 mRNA expression; TNF with DMSO vs. TNF with MG132, 4.9 fold vs. 2.0 fold).

| Name of Inhibitor | Signaling pathway | Inhibitory Rate (%) |
|---|---|---|
| Kenpaullone | CDK | 60.4 |
| AG1024 | IGF-IR | 60.8 |
| purvalanol A | CDK | 60.8 |
| NU6102 | CDK | 61.8 |
| GSK-3 inhibitor IX | GSK | 65.3 |
| Lavendustin C | CAMKII | 70.6 |
| SU4984 | FGFR | 71.5 |

**Conclusion:** We identified GSK3 pathway as one of the novel target to PDAC. Downregulation of PD-L1 may sensitize the effect of anti-PD-1 therapy as well as restoring anti-tumor immunity in PDAC. These data suggested that inhibition of PD-L1 by using certain protein kinase inhibitors could be a potential therapeutic option as a combined therapy with the current anti-PD-1 antibody against pancreatic cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1200 CUX1 COOPERATES WITH K-RAS IN THE TUMOR PROGRESSION OF PANCREATIC CANCER IN VIVO

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**Introduction:** The transcription factor CUX1, a regulator of cell differentiation and cell cycle progression, supports cell migration and resistance to apoptosis in vitro and in a xenograft model in vivo. The impact of CUX1 on tumor progression in a genetic mouse model of pancreatic cancer has not been elucidated.
**Aims & Methods:** Aim: Analysis the effect of CUX1 on tumor progression in vivo and molecular characterization of effector signaling cascades. Methods: A transgenic mouse model expressing CUX1 under the control of the CMV-promotor was crossbred with a pancreatic PanIN mouse model expressing constitutively active K-Ras under the control of the pancreas-specific p48 promotor (p48-Cre;LSL-KRASG12D). Subsequently, PanIN burden and tumor incidence was examined, as well as the regulation of CUX1 dependent signaling cascades in the context of K-Ras activation.
**Results:** The transgenic CUX1 expression in cooperation with pancreas-specific K-Ras activation caused a significant increase of PanIN lesions and invasive carcinomas. This correlates with a significantly enhanced proliferation rate in vivo and increased colony formation of CUX1 expressing cells in the presence of activated K-Ras in vitro. Interestingly, CUX1 significantly synergizes with K-Ras by inducing activation of MEK/ERK signaling, which occurred exclusively in the presence of activated K-Ras.
**Conclusion:** The in vitro und in vivo data show cooperation of CUX1 and K-Ras dependent pathways, resulting in an enhanced MEK/ERK signaling pathway leading to acceleration of pancreatic carcinogenesis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1201 THE FEATURES OF HOST IMMUNE RESPONSE IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

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**Introduction:** Despite the development of diagnostic imaging and treatment, pancreatic ductal adenocarcinoma (PDAC) remains the lethal malignancy with extremely poor prognosis. Surgical resection is the only treatment achieving radical curation; however, only 15–20% of patients are diagnosed in the operable early stage. For unresectable PDAC patients, chemotherapy is efficacious; however, improvements in survival are extremely limited.
**Aims & Methods:** It is extremely important to understand the host inflammatory immune response of PDAC for development of novel diagnostic tool as well as therapy. In the current study, we examined the local immune response of 20 PDAC tissues resected by surgery assessed with immunohistochemistry (IHC). Next, we analysed gene expression profile for CD4+cells, CD8+ cells, CD14+ cells and CD15+ cells in peripheral bloods by DNA microarray, which are obtained from five PDAC patients (Age; $76.6 \pm 11.2$, Gender; Male/Female=5/0, Stage I/II/III/IV = 0/3/1/1) and seven healthy volunteers (Age; $61.7 \pm 3.9$, Gender; Male/Female = 3/4). Furthermore, we examined surface antigens expressed on CD4+ cells and CD14+ cells to characterize the subpopuplation of these cells in PDAC patients by flow cytometry.
**Results:** We observed that CD4+ cells were abundantly infiltrated in PDAC focal site, compared to CD8+ cells in T cells. In infiltrated CD4+ cells, PD-1, immune checkpoint molecule, as well as FoxP3, master molecule of regulatory T cell, were prominently expressed, compared to T-bet, master molecule of helper T cell. Furthermore, we observed CD33+ cells, phenotypic of myeloid cells, were significantly infiltrated in focal tumor site, and most CD33+ cells also expressed CD163+ cells, suggesting M2 like macrophages. The gene expression profile of peripheral blood CD4+ T cells and CD14+ monocytes was discernible between PDAC patients and healthy volunteers, although CD8+ cells and CD15+ cells were not. 496 genes whose expression was significantly different in CD4+ T cells of PDAC patients were related to the cell cycle and inflammation as well as DNA damage and apoptosis, and 261 genes those of CD14+ monocytes in PDAC patients were related to the cell cycle, inflammation, blood coagulation, cell adhesion and development. Flow cytometric analysis showed that the frequency of molecules related to immune

suppression, which were CD4+PD-1+ cells, CD4+CD25+CD127+ cells and CD11b+CD33+ cells was significantly increased in both CD4+ cells and CD14+ cells of PDAC patients.
**Conclusion:** Immune reaction including immune-suppression-related molecules and cells were indicated in systemically circulating peripheral blood cells as well as local cancer tissues in PDAC patients. These findings are useful for understanding immune condition of PDAC for exploration of novel diagnostic tool as well as novel immunotherapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1202 EXHAUSTIVE ANALYSIS OF MICRORNAS IN THE PANCREATIC CANCER TISSUE OBTAINED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA)

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**Introduction:** MicroRNAs (miRNAs) which is small molecule RNA conducts translation suppression of the target molecule and is associated with the molecular mechanism of cancerogenesis and the extension process deeply. The pancreatic cancer, is one of the refractory gastrointestinal carcinoma, has difficulty in early detection, and the metastasis of tumor cells, an invasion tendency are strong, and the treatment resistance. Recently, there are some reports that the microRNAs have been associated with these refractory characteristics in the pancreatic cancer. Therefore, we examined likelihood of the clinical application by the analysis of miRNAs in the tissue of the pancreatic cancer obtained by EUS-FNA.
**Aims & Methods:** A total of 51 consecutive patients (21 men and 30 women, mean age 67.9) underwent EUS-FNA for pancreatic tumor from April, 2013 to February, 2016. They were all diagnosed pancreatic ductal adenocarcinoma by the cytopathologist. Firstly, the pancreatic cancer tissue obtained by EUS-FNA was cryopreserved using RNA stabilization reagnet (RNA later, Qiagen). After total RNA extraction, we exhaustively analyzed expression of microRNAs using microRNA array tip (TORAY company) which approximately 2,500 molecules were put on.The statistical analysis assumed a significant difference ($p$ value $< 0.05$) using Wilcoxon signed-rank test.
**Results:** In the comparison of the microRNAs between resection group (13 cases) and non-resection group (38 cases), 92 genes showed a significant difference. In comparison of the microRNAs between the locally advanced group and the each metastatic group (liver metastases 17 cases, lung metastases 4 cases, lymph node metastases 9 cases), 326, 32 and 164 genes showed a significant difference, respectively. Oncogenic microRNAs indicating the overexpression, tumor suppressor microRNAs indicating the expression decrease were identified in each. Furthermore, microRNAs at the time of pancreatic cancer diagnosis were also observed that seems to be related with the site of recurrence in the post-operative patients.
**Conclusion:** Analyzing miRNAs exhaustively extracted by EUS-FNA at the diagnosis, we identified miRNAs which prescribed the clinical features of the pancreatic cancer. In the future, we want to examine clinical application of these microRNAs as the biomarker of the pancreatic cancer used for a diagnosis, a prognostic value and an effect of treatment judgment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1203 EFFECTS OF ARGININE–GLYCINE–ASPARTIC ACID PEPTIDE CONJUGATED QUANTUM DOTS INDUCED PHOTODYNAMIC THERAPY ON PANCREATIC CARCINOMA IN VIVO

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**Introduction:** Pancreatic cancer is currently one of the deadliest of the solid malignancies. Overall prognosis is poor with palliative chemotherapy and/or radiotherapy. Photodynamic therapy (PDT), a minimally invasive treatment capable of local destruction of tumor tissue may have a place in the treatment. Quantum dots (QDs) are colloidal semiconductors. Arginine-glycine-aspartic acid (RGD), sequence of small peptide, is an integrin antagonist which can link to integrin of cancer cells. We successfully combined the construction of RGD conjugated quantum dots (QDs-RGD). Our previous studies have showed the potential applications of QDs-RGD for PDT as photosensitizers in pancreatic cancer cells in vitro. In this study we investigated its applications for PDT in pancreatic carcinoma bearing mice.investigated its applications for PDT in pancreatic carcinoma bearing mice.
**Aims & Methods:** Nude mice were subcutaneously injected with SW1990 pancreatic cancer cells on the back. The mice were maintained with regular food and water, until the tumor volumes approached 500–1000mm$^3$. Different dosages of QDs-RGD, such as 0.1 pmol, 0.2 pmol, 0.5 pmol, 1 pmol, 2 pmol, 5 pmol, 10 pmol, 20 pmol, 50 pmol, were dissolved in 100 $\mu$L of sodium borate. Then they were injected into the tumor-bearing mice intratumorally or intravenously. In vivo optical imaging was performed with the IVIS Imaging System. Images were acquired at different time points after injection, including 0 h, 1 h, 3 h, 5 h, or 24 h. PDT was performed with an optical fiber directly injected into the tumor connecting the laser light asset. For the PDT group (group 1), mice were intratumorally injected with 5 pmol of QDs-RGD and then irradiated for 20 min with laser light (630 nm) at a power density of 100mW/cm$^2$. The control groups included mice that received a QDs-RGD injection at the same dose but were not irradiated (group 2) and mice that did not received a QD-RGD injection but were irradiated (group 3). The tumor sizes were measured using a caliper every other day. All the procedure above was performed once again on the 14$^{th}$ day. Mice were sacrificed at the 28$^{th}$ day and histology analyses of tumor tissues were performed. Tumor tissues were separated and embedded in paraffin. The sliced tumor tissues were stained with hematoxylin–eosin (H&E).
**Results:** When the dosages of QDs-RGD were lower than 1 pmol, neither the intratumorally injected group nor the intravenously group could maintain in the tumor with a high level of Fluorescence Radiant Efficiency. When the dosages of QDs-RGD reached 5 pmol or above, the intratumorally injected QDs-RGD group could maintain in the tumor with a high level of Fluorescence Radiant Efficiency for at least 3 hours, while the efficiency of the tumor in the intravenously group still retained low. After the PDT treatment, tumors on the back of the mice in group 1 grew slowly, whose average $V/V_0$ ratio is 3.36, while in the control group (group 2 and 3), tumors grew fast with their average $V/V_0$ ratios could reach 13.46 and 16.66, which means tumors could grew to 16 times of its previous size within 4 weeks. The H&E results of tumor tissues showed that there are more necrotic tissues, more inflammatory cells, and less vascular tissue in tumor tissue of intratumorally PDT groups (group 1) as compared to control without treatment (group 2 and 3).
**Conclusion:** These results indicated that intratumorally injected QDs-RGD could achieve high Fluorescence Radiant Efficiency in the tumor of nude mice. QDs-RGD-mediated PDT, with the illumination of an optical fiber directly inserting into the tumor, is able to destroy the growth of SW1990 tumors with high efficiency in nude mice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1204 A GLYCOPROTEIN AS A NOVEL SEROLOGICAL MARKER FOR PANCREATIC CANCER

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**Introduction:** Accurate peripheral markers for the diagnosis of pancreatic ductal adenocarcinoma (PDAC) are lacking. Biomarkers for the diagnosis of patients with PDAC are needed to improve prognosis.
**Aims & Methods:** The aim of the present study is to assess if a glycoprotein which we found in condition media of cultured human PDAC cells is useful as a serum diagnostic marker for differentiating PDAC from individuals without pancreatic disorders compared with cancer antigen 19–9 (CA19–9). A case-control study included two subcohorts: the discovery cohort that included 23 PDAC patients (stage 0: n = 1, IIA: n = 2, IIB: n = 4, III: n = 6 and IV: n = 10 according to the classification of International Union against Cancer) and 51 control individuals, and the validation cohort that included 29 PDAC patients (stage IA: n = 1, IIA: n = 7, IIB: n = 16, III: n = 3 and IV: n = 2) and 14 control individuals. PDAC patients and control individuals who were treated in Kochi Medical School Hospital and Kochi Health Sciences Center were included from April 2014 to March 2015 in the discovery cohort and from April 2015 to January 2016 in the validation cohort. The serum glycoprotein was measured by a commercial sandwich ELISA kit.
**Results:** The discovery cohort demonstrated that the area under the receiver-operating characteristic curve (AUC) were 0.973 (95%CI 0.943–1) for this glycoprotein and 0.802 (95%CI 0.693–0.912) for CA19–9. The AUC for the glycoprotein was significantly higher than that for serum CA19–9 (P = 0.004). The validation cohort showed the similar results of the discovery cohort.
**Conclusion:** Our data suggest that measuring the level of this glycoprotein has the potential to improve detection of PDAC. Further research is necessary to confirm its value for early detection of PDAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1205 THE ACTUAL INCIDENCE OF PANCREATIC CYSTIC NEOPLASM RELATED SYMPTOMS: WE ARE OVERESTIMATING A MAJOR INDICATION FOR SURGERY

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**Introduction:** The treatment of pancreatic cystic neoplasms (PCNs) relies on several International guidelines that identify key features able to predict the

risk of malignancy. The most important of these factors is represented by the presence of symptoms. The incidence of symptomatic PCNs is based on retrospective series that might overestimate the actual incidence and consequently lead to inappropriate indication for surgery.
**Aims & Methods:** To evaluate the actual PCN related symptoms incidence and profile. Patients affected by PCNs (n = 108) observed between September 2015 and February 2016 were prospectively enrolled. All patients underwent physical examination, MRI with cholangiopancreatography and a specific interview on gastrointestinal (GI) symptoms. An identical survey was carried out on a matched control population (n = 98) in which the presence of PCNs or other pancreatic focal lesion were excluded by MRI with cholangiopancreatography.
**Results:** The study group showed an increased prevalence of female subjects (66.7 vs. 43.9%, $p < 0.01$) and a higher median age (64 vs. 56 years, $p < 0.01$), while matched with the control group regarding comorbidities. There was no difference in terms of incidence of GI symptoms. Of note, abdominal pain was reported in 61% of subjects with and in 51% of subjects without PCNs ($p = 0.1$). Patients with PCNs were more aware of their symptoms being able to better characterize them in relation with food intake and sleep. Same results were obtained comparing patients with BD-IPMN (53.7%) and the control group. Seven patients with PCN (6.4%) have been proposed for surgery due to the presence of worrisome features or high risk stigmata, however, none of this patients experienced symptoms.
**Conclusion:** Subjects affected by PCNs have similar GI symptoms incidence and profile if compared with individuals without pancreatic disease. Care must be taken recommending surgery for PCNs due to the presence of symptoms, as these might not be actually related to the cyst itself.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1206 DIGITAL SINGLE OPERATOR PANCREATOSCOPE (DSOP) IN PANCREATIC INTRAPAPILLARY MUCINOUS NEOPLASIA (IPMN)


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**Introduction:** Precise knowledge of the extent of disease guides the surgical management of IPMN. We hypothesized that preoperative DSOP alters the operative plan in patients with IPMN.
**Aims & Methods:** A multicenter retrospective review of 16 patients who had DSOP attempted for IPMN was performed. A single-use, multi-purpose 10.5 Fr flexible endoscope, all-inclusive design with independent irrigation and a 1.3 mm therapeutic channel (SpyGlass DS$^{tm}$, Boston Scientific, MA, USA) was used in an outpatient setting under monitored anesthesia, without prophylactic antibiotics and without sphincterotomy in 13 cases; The duct was swept with a balloon prior to ductoscopy. Standard imaging findings, endoscopic findings, surgical treatment and pathology were reviewed.
**Results:** DSOP was performed in 16 patients with pancreatic IPMN, 11 men, 5 women, mean age 72 years. The majority (13) had main duct IPMN and 3 had mixed-IPMN (main duct and branched). DSOP was successfully performed in 15/16 patients reaching the tail (One patient had an alpha-loop in the head). The location of the IPMN by imaging studies was in the head (5), body (8), and tail (3). Endoscopic findings included: mucin extruding from the ampulla (14), villiform protrusions with a transparent appearance (15), villiform protrusions with central vessel (13), nodules (13), luminal mucin (14), "fish-egg" appearing side branches (9), and stones (1). In the patients with a tail mass, the remainder of the duct was normal. In patients with a distal mass (head/body/neck), the proximal duct appeared hyperemic, with prominent vascular surface, subepithelial edema, nodules and shallow villi to the tail (10). Compared to standard preoperative imaging, DSOP further extended the location of the tumor in 8/13 (61%). Biopsies (SpyBite$^{tm}$, Boston Scientific, MA, USA) were performed in 14 revealing mucinous lesion (14), low grade and high grade dysplasia (5 and 3, respectively). In one patient with a mass in the tail, biopsies of the distal duct showed dysplasia despite a normal appearance. Ten patients underwent surgery, 4 showing early adenocarcinoma and 5 showing high-grade dysplasia: all these patients had central vessels in the villi. The pre- DSOP surgical approach was modified in 6/10 of the patients (3 pancreatoduodenectomy versus total pancreatectomy; 1 total pancreatectomy instead of pancreatoduodenectomy. Complications included one patient with mild pancreatitis requiring an overnight hospitalization.
**Conclusion:** DSOP with biopsy in IPMN reveals more extensive disease than standard preoperative imaging and frequently alters the surgical plan particularly in patients with lesions in the head of the pancreas where dysplastic changes are noted throughout the duct. Villi with central vessels may be associated with more advanced disease.
**Disclosure of Interest:** I. RAIJMAN: Speaker, Boston Scientific Corporation Speaker, ConMed Speaker, Covidien Speaker, Takeda Pharmaceuticals
R. Shah: Advisory board and consultant, Boston Scientific Corporation
P. Tarnasky: Consultant and speaker, Boston Scientific Corporation
M. Othman: Speaker, Abbvie Speaker, Olympus Corporation Speaker, Medtronic
M. Kahaleh: Advisory board and consultant, Boston Scientific Corporation Speaker, Pinnacle Speaker, Emcision Speaker, Gore Speaker, Olympus Corporation of America
S. Patel: Speaker, Boston Scientific Corporation Speaker, ConMed
D. Nguyen: Speaker, Abbvie
All other authors have declared no conflicts of interest.

### P1207 THE FEASIBILITY OF TISSUE SPECIMEN OBTAINED FROM EUS-FNA FOR PATIENT-DERIVED TUMOR XENOGRAFT IN PANCREATIC CANCER


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**Introduction:** There has been an increasing interest in the development and characterization of patient-derived tumor xenograft (PDX) models for cancer research. Although most of the published studies have relied on surgical specimens, it is difficult in pancreatic cancer because most patients were initially diagnosed as advanced stage and surgically inoperable. The aim of our study is to evaluate the feasibility of PDX using EUS-FNA specimens in pancreatic cancer.
**Aims & Methods:** Patients were referred for EUS-guided tissue acquisition were prospectively enrolled. Among them, patients with locally advanced or distant metastasis were included. After the acquisition of tissue specimen for pathologic diagnosis, additional EUS-guided tissue sampling was performed for xenograft and storage for further DNA analysis. The acquired FNA specimen was implanted subcutaneously into the dorsal region of athymic nude mouse. We evaluated the success rate of implantation and compared the histologic correlation between human tumor and xenograft mass.
**Results:** Between April 2014 and January 2015, 10 patients (median age, 69 years; range 47–79; male:female ratio, 7:3) were enrolled and all were diagnosed as pancreatic cancer by EUS-tissue sampling. The mean size of tumor was $32.7 \pm 15.3$ mm by $25.6 \pm 9.2$ mm. Tumor formation was observed in two cases (20%) at 3 week and 5 week after implantation. Finally, it took 6 weeks and 21 weeks until the growth of 1 $cm^3$ in volume. In successful xenograft tissues, histologic and immunohistochemical staining revealed identical pathologic findings to those of the human tumor.
**Conclusion:** With the successful PDX using EUS-FNA specimen in pancreatic cancer, we expect that this may contribute to the development of a tailored therapy for pancreatic cancer in the future. However, further studies are required to shorten the growth period to obtain a sufficient volume of xenograft before applying clinical management.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1208 EARLY VERSUS DELAY INITIATION IN ADJUVANT TREATMENT FOR PANCREATIC CANCER

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**Introduction:** Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive tumor with a tendency for early recurrence, even after curative resection. Although adjuvant treatment improves survival, it is not well described early initiation of adjuvant therapy shows better outcomes in patients with PDAC.
**Aims & Methods:** One hundred thirteen patients who underwent chemotherapy or chemoradiotherapy after curative resection of PDAC were enrolled retrospectively: 56 in early group and 57 in delay group according to the median value of the time to initiation treatment.
**Results:** The median time to start adjuvant treatment was 34 days (range, 20 – 83 days), and 71 patients underwent adjuvant treatment completely. The median overall survival was 39.1 vs. 21.1 months, and disease-free survival was 18.8 vs. 10.0 months in the early and delay groups, respectively ($p = 0.018$ and 0.034), during the median 20.3-month follow-up. Also, the overall and disease-free survival rate of the early group tends to be higher than those of the delay group in whom underwent complete adjuvant treatment ($p = 0.129$ and $= 0.195$, respectively). On multivariate analysis, an incompletion of therapy (hazard ratio [HR]: 4.536, 95% confidence interval [CI]: 2.570 – 8.005), delay initiation of therapy (HR: 2.042, 95% CI: 1.178 – 3.541), and positive angiolymphatic invasion (HR: 2.135, 95% CI: 1.143 – 3.988) were significantly associated with shorter overall survival.
**Conclusion:** Adjuvant treatment would be delivered earlier and completed for better outcomes after curative resection of PDAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1209 RESECTABLE PANCREATIC CANCER: ARE WE PERFORMING A GOOD PRE-OPERATIVE STAGING?

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**Introduction:** Pancreatic cancer (PC) is the gastrointestinal cancer with the lowest survival rate. Therefore it is essential to provide the best treatment for each disease stage, this is the reason why it is crucial to perform a proper staging [1].
**Aims & Methods:** The aim was to compare the correlation between the pre and post-operative staging through various imaging methods. This is a single-center retrospective study (2010–2015) including all the patients proposed to surgical resection for PC. Agreement analysis was performed through specific proportion. Statistics analysis was performed using IBM SPSS Statistics 22 with $p < 0.05$ deemed to be statistically significant.
**Results:** We identified 77 patients, 57.1% male, with a mean age of 67.0 years (IQR: 58.5–72.0) at diagnosis. The median survival period was 12.0 months (IQR: 8.0–25.5). The staging of PC was performed in 96.1% patients by computed tomography (CT), 24.7% patients by endoscopic ultrasound (EUS) and in 20.8% patients by both methods. Before surgery, most of the patients belonged to stages IIb (25.3%) and IIa (24.0%); Surgical and post-operative staging revealed that the majority of patients belong to stage IIb (32.9%) and IIa (25.0%). Nineteen percent of the patients enrolled showed non-resectability criteria at the time of surgery, 70.6% due to locally advanced disease. Patients not resected had performed pre-operative staging by EUS and CT in 35.3% and 94.1%, respectively. Considering patients who underwent staging by EUS, 31.6% had no resectability criteria at the time of surgery, and this occurred in 31.2% of patients whose staging was performed by CT. According to TNM Classification, the concordance between the pre and post-operative staging with CT was: T (56.3%) and N (39.7%); EUS: T (52.4%) and N (53.8%). The agreement between the pre and post-surgery staging was not associated with more than one imaging method, location and/or size of the lesion.
**Conclusion:** Pre and post-operative staging showed low agreement using CT and EUS. Performing more than one imaging method has not determined an increase in the accuracy of TNM staging.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1210 VALUE OF CA 19–9 LEVELS FOR PANCREATIC CANCER SCREENING IN NEW-ONSET DIABETIC PATIENTS REGARDLESS OF BILIRUBIN ELEVATION

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**Introduction:** Early check-up of CA 19–9 could be a useful marker for screening for pancreatic cancer (PC) in asymptomatic patients with new-onset diabetes mellitus (DM). However, PC group had significantly higher bilirubin levels, which could be the confounding factor for evaluating screening tool of CA 19–9.
**Aims & Methods:** This study aims to confirm the utility of measuring CA 19–9 in asymptomatic new-onset diabetic patients as a screening test for PC, independent of bilirubin elevation. Patients who newly diagnosed with DM and measured CA 19–9 at Korea University Guro Hospital health promotion center from January 2005 to January 2014 were enrolled. Medical records of patients were reviewed retrospectively, Statistical analyses were performed using $\chi^2$ tests, independent two tailed T-tests and area under ROC curve.
**Results:** In the 5111 patients (male 64.2%, mean 60.3 years) selected for analysis, 87 (1.7%) patients developed PC after the DM diagnosis. There was no statically significant difference in the clinical profiles of patients, including age, sex, smoking history, BMI, glucose, HbA1C, liver function test, and CEA between the PC group (87 patients) and non-PC group (5024 patients). However, CA 19 -9 level and bilirubin were significantly higher in the PC group than non-PC group. In the subgroup of 322 patients with elevated bilirubin (1.7 mg/dL), 42 (73.7%) of 57 patients with elevated CA 19–9 level ($>$ 37 IU/mL) were finally diagnosed with PC. The other 265 patients were checked normal CA 19–9, and 12 cases (4.5%) of them showed PC (OR 16.3, 95% C.I. 8.06 to 32.8; $P < 0.001$). In the other subgroup of 4789 patients with normal bilirubin, 20 (3.8%) PC in 522 patients with elevated CA 19–9 and 13 (0.3%) PC in 4267 patients with normal CA 19.9 were finally detected (OR 12.6, 95% C.I. 6.22 to 25.43; $P < 0.001$).
**Conclusion:** Check-up of CA 19–9 following new-onset DM diagnosis could be a useful marker as a screening test for pancreatic cancer, independant of bilirubin elevation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1211 CONTINUOUS LOW-DOSE-RATE IRRADIATION OF IODINE-125 SEEDS INHIBITS PERINEURAL INVASION IN PANCREATIC CANCER

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**Introduction:** Perineural invasion (PNI) extending into the extrapancreatic nerve plexus is a histopathologic characteristic in pancreatic cancer. The proper treatment of neural invasion has not been established. According to the valuable observations in the previous clinical studies, we established the PNI models of pancreatic cancer in vivo and in vitro, observed the treatment effect of continuous low-dose-rate (CLDR) irradiation to PNI and assessed PNI-related pain relief caused by 125I seeds implantation.
**Aims & Methods:** Aims: To observe the treatment effect of continuous low-dose-rate (CLDR) irradiation to perineural invasion with iodine 125 seeds implantation. Methods: The in vitro PNI model established by co-culture the dorsal root ganglion (DRG) with cancer cells was interfered under CLDR irradiation of 2 and 4 Gy. The subcutaneous and orthotopic models of PNI were established and iodine 125 seed was implanted in the tumor. The PNI related molecules were analyzed. In 31 patients, the pain relief was assessed using a visual analogue scale (VAS). Pain intensity was measured before and 1 week, 2 weeks, 1, 3, 6 months after implantation.
**Results:** In co-culture groups, the increased number of DRG neurite and pancreatic cell in radiation group was significantly less. In subcutaneous models, the PNI positive rate in radiation and control group was 33.3% (4/12) and 80% (8/10) ($P < 0.05$). In orthotopic models, the PNI degree between radiation and control group was significantly difference. At week 2, the average pain score in patients decreased by 50%. The pain scores were lower in all patients and the pain-relieving effect was retained about three months.
**Conclusion:** The CLDR irradiation could inhibit PNI of pancreatic cancer with the value of further study. The CLDR irradiation could do great favor in preventing local recurrence and alleviating pain.
**Disclosure of Interest:** All authors have declared that they have no competing interests.

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## P1212 MENSTRUAL AND REPRODUCTIVE FACTORS AND RISK OF PANCREATIC CANCER IN WOMEN

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**Introduction:** Pancreatic cancer (PC) is a deadly disease with a 5-year survival of less than 5%. Worldwide PC incidence rates are lower among women than men. While this suggests a protective role for steroid hormones in PC risk, results from epidemiologic studies are not consistent.
**Aims & Methods:** Odds ratios and 95% confidence intervals for reproductive factors and PC were estimated using Logistic regression methods in a prospective case –control study. A hundred sixty-seven new incident PC cases and 198 controls were both recruited in the study from a referral center for endoscopic ultrasound between 2011 and 2016. A structured valid and reliable questionnaire was used for data collection by trained interviewers.
**Results:** Mean age (SD) of cases and controls were 63.8 (11.8) and 63.5 (12.0) years respectively. Age at menarche, age at menopause, number of parity, gravidity and abortion were not associated with PC risk.
**Conclusion:** This study does not support for the hypothesis that menstrual and reproductive factors are associated to PC risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1213 EUS-ELASTOGRAPHY (STRAIN RATIO) IN THE DIAGNOSIS OF SOLID PANCREATIC LESIONS: A PROSPECTIVE COHORT STUDY

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**Introduction:** Preoperative diagnosis of solid pancreatic masses (SPL) is a challenging clinical problem. EUS elastography is a non-invasive ultrasound technique that displays the relative stiffness of tissues by taking advantage of the deformation caused by the compression or vibrations of the tissues. The level of hardness of SPL can be evaluated using either a qualitative scores and/or quantitative methods (strain ratio; SR).
**Aims & Methods:** This single-center prospective cohort study aimed to evaluate the feasibility and efficacy of the combination of EUS elastography and SR in the diagnosis of SPL by using the elastography software on the new Olympus compact ultrasound processor EU-ME2 in association with the linear array Olympus GF-UCT-180 series echoendoscopes. Two different areas were selected for SR. Area A was a representative area of the mass and included the biggest possible area of the tumor. Area B was placed in a soft peri-tumoral normal parenchyma to calculate the pSR and in the GI wall to calculate the wSR. The quantitative score of elastography was calculated by the SR method, dividing the non-mass soft tissue area (area B) by the tumoral area (area A). Every time, 3 measures of SR for pSR and wSR were recorded and the mean value for each was calculated and used as final SR result for each lesion. Patients with SPL detected by CT or MRI and confirmed by EUS, with age >18 years, were included. Procedures were performed between February 2016 and April 2016. Informed consent was obtained from all patients. The hospital institutional review board approved the study. Final diagnosis was made on the basis of EUS-FNA, surgical specimens, and follow up.
**Results:** Study population included 28 patients: 15 male and 13 female (mean age 69 years). The mean size of SPL was 26.5 mm (SD 13.7). The localization was the tail in 10 (35.7%), body in 10 patients (37.5%), neck in 3 (10.7%), head in 8 (28.6%), uncinated process in 4 (14.3%). Twenty-three patients underwent EUS-FNA. The adequacy was obtained in all patients (96%) but one with suspected autoimmune pancreatitis. The mean number of passages was 2 (SD 0.8; range 1–3). Final diagnosis was pancreatic ductal adenocarcinoma (PDAC) in 18 patients, NET in 4 patients. Two of 5 SPL without FNA were suspected for NET, and the lesions were stable compared to previous EUS or radiological imaging. The other two lesions showed a solid component of degenerate cystic neoplasm confirmed by surgery. An other LST was an inhomogeneous area in a patient with past acute pancreatitis, stable after 6 months follow up. SR was feasible in all patients with both methods, pSR and pSR. The patient with suspected autoimmune pancreatitis, without a final diagnosis, was excluded from the study. The mean pSR of PDAC, NET and non neoplastic SPL was respectively 26, 11 and 2. The mean wSR of PDAC, NET and non neoplastic SPL was 47.5, 15, and 10. The major limitation of this study is the low n° of benign mass, but these preliminary data showed the feasibility of the SR calculated with the Olympus EU-ME2 echo-processor and the higher SR values in PDAC.
**Conclusion:** EUS-elastography may add information in the EUS assessment of SPL, especially in the identification of lesion suspected for PDAC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**ENDOSCOPY AND IMAGING III – POSTER EXHIBITION**

## P1214 ENDOSCOPIC DUODENAL MUCOSAL RESURFACING TREATMENT FOR TYPE 2 DIABETES: EARLY MULTICENTRE EXPERIENCE

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**Introduction:** Bariatric surgery improves the metabolic state of subjects with type 2 diabetes (T2D) through weight-independent mechanisms. Duodenal mucosal resurfacing (DMR) is an investigational endoscopic procedure involving novel balloon catheter-based thermal ablation of duodenal mucosa. An initial single-site, first-in-human (FIH) study in Chile has reported robust improvements in glycaemic control after DMR among a cohort of subjects with T2D.
**Aims & Methods:** We report the early safety, feasibility, and efficacy of implementing DMR in an European multi-centre study (5 sites) in subjects with T2D. At study sites, endoscopists received a day of both didactic and hands-on DMR training in a porcine model before treating subjects with T2D, sub-optimally controlled (HbA1c 7.5–11.0%) on oral glucose-lowering medication. DMR involved duodenal lumen measurement, mucosal lifting with a submucosal expansion catheter followed by circumferential mucosal ablation (length ~8 cm) with a thermal ablation catheter. Subjects on sulfonylurea (SU) medication had their SU withdrawn 4 weeks prior to procedure to mitigate hypoglycaemia potential. All subjects followed a graduated diet for 2 weeks post-procedure and a proton pump inhibitor was prescribed for 5 weeks.
**Results:** Twenty-eight subjects (age $55 \pm 9$ years, baseline HbA1c $8.7 \pm 1.0$%, BMI $32.3 \pm 4.3$ kg/m$^2$) received DMR treatment with current follow-up of 12 weeks post-procedure for the full cohort and some subjects currently followed for 24 weeks. The procedure was implemented according to protocol and well tolerated by all subjects. There were no procedure-related severe adverse events including no duodenal stenoses. Adverse events have been mostly mild in severity. Metabolic indices improved significantly 12 weeks after DMR (change from baseline lowering of FPG 31 mg/dL, HbA1c 0.7%, ALT 7.7 IU/L) despite protocol-driven withdrawal of SU therapy in the majority of subjects prior to DMR. BMI decreased significantly by 0.9 kg/m$^2$ during 12 weeks after DMR.
**Conclusion:** The DMR procedure is a novel endoscopic catheter-based treatment for the management of T2D and current clinical use suggests that the procedure can be implemented in a multi-centre setting. This study reports a favourable safety and tolerability profile observed to date with further evidence of the improved glycaemic and hepatic measures elicited by DMR. Further

assessment of clinical applicability, and efficacy and safety of the DMR procedure is necessary.

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M. Passos Galvão Neto: Serves on the scientific advisory board of and receives research funding from GI Dynamics, Inc., and Fractyl Laboratories, Inc.
L. Rodríguez: Research suport from Fractyl Laboratories, Inc
R.J. Haidry: Educational Research grants from Cook Endoscopy and Pentax Medical Europe to support research infrastructure
J.J. Bergman: Research supp.: Olympus Fujifilm Cook Boston Scientific GI Solutions Covidien Erbe Ninepoint C2 Cernostics Interpace Fractyl. Honorarium-consultancy-speakers fee: Cook Boston GI Solutions Covidien
All other authors have declared no conflicts of interest.

## P1215 TRANSFUSION STRATEGY AND DEATH RISK IN PATIENTS WITH ACUTE NON VARICEAL UPPER GASTRO INTESTINAL BLEEDING (NV-UGIB) IN ITALY: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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**Introduction:** Acute non-variceal upper gastrointestinal bleeding (NV-UGIB) is a frequent indication for hospital admission and blood transfusions; meta-analysis and randomized controlled trials examining red blood cell (RBC) transfusions for the management of NV-UGIB were inconclusive and the appropriate strategy for transfusions in patients with haemorrhage and haemoglobin (Hb) value between 7 and 9 gr/dl is still unclear.

**Aims & Methods:** We aim to evaluate the impact of different transfusion strategies on death risk in patients admitted for NV-UGIB focusing on haemoglobin (Hb) value between 7 and 9 gr/dl Data on patients admitted for GI bleeding were collected from January 2014 to January 2016. 30-day mortality and type of transfusion strategy adopted were the primary outcomes measured. Transfusion strategy definitions: "restrictive" for Hb levels $\leq$7 g/dL; "not justified" (depending on symptoms) for Hb levels from 7 to 9 gr/dL; "liberal" for Hb levels from 9 to 10 gr/dL; "not indicated" for Hb levels $\geq$ 10 gr/dL. All participating centres were free to follow the transfusion strategies approved in their own hospital. Mortality was defined as any death occurred within 30-day from admission.

**Results:** A total of 3224 patients were included. Of these 2,764 (83.1%) had NV-UGIB (mean age 69.1 $\pm$ 16.2, 67.8% males). Comorbidities were present in 79.8% of the patients, the mean Rockall score was 3.9 $\pm$ 1.9. At admission, mean Hb value was 9.2 $\pm$ 2.6 and 7.6% of the patients had hemodynamic instability. 58.2% of the patients were transfused, receiving a mean of 3.1 RBC units per patient with a 30-day mortality of 5.6%. Overall, a total of 5015 units were transfused, 2629 in the restrictive group, 2053 in the "not justified" or "not indicated" groups, while 333 units were administered without any indication. Transfusions impacted on mortality, being statistically different between those who received any RBC unit vs those who did not (7.7% vs 2.9% $p < 0.000$); the death risk varies considerably within the Hb strata value (tab.1). 43% of the patients had a "restrictive" transfusion strategy, 39% a "not justified" strategy, 4.9% the liberal transfusion and 3% the transfusions were not indicated. Considering only the "not justified" group, after transfusions, 93 out 1084 patients still had an Hb value $\leq$ 8 gr/dl with a mortality rate of 23.6% [vs. 6.8% of the other groups ($p < 0.000$) ]. Both in the group <= 7 g/dl and in that 7–8 g/dl those in which the average value of Hb has exceeded 8 g/dl mortality has decreased substantially and fluctuated between 5.5 and 8.6% ($P = 0.24$).

**Conclusion:** In patients with NV-UGIB the "not justified" strategy must be reconsidered for the substantial death risk. A transfusion strategy to achieve a target Hb value ranging from 8 to 9 gr/dL is advisable.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1216 PERORAL ENDOSCOPIC MYOTOMY FOR TREATING ACHALASIA PERFORMED BY A GASTROENTEROLOGIST: 4 YEARS' EXPERIENCE FROM A SINGLE ENDOSCOPY CENTER

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**Introduction:** Esophageal achalasia is most commonly treated with endoscopic dilation or laparoscopic Heller myotomy. Peroral endoscopic myotomy (POEM) has recently been described as a novel treatment for achalasia in humans.

**Aims & Methods:** The aim of this study was to assess the clinical effectiveness and safety of POEM for treating esophageal achalasia performed by a gastroenterologist in a single endoscopic center within 4 years. Between June 2011 to May 2015, POEM was performed in 115 consecutive patients with achalasia. POEM procedure consisted of the following step: firstly, submucosal tunnel was created and extended below the lower esophageal sphincter (LES) onto the gastric cardia after a mucosal incision was made; then endoscopic myotomy of circular muscle bundles was done; finally, the mucosal entry was closed by hemostatic clips. The Eckardt score and manometry were used to evaluate the outcomes. Treatment success was defined as symptom relief, based on an Eckardt score $\leq$ 3.

**Results:** POEM was successfully performed in all cases. Mean procedure time was 48.7 min (range 35–93) and mean myotomy length was 9.2 cm (range 7–15). Mucosal perforations occurred in 7 (6%) patients during submucosal tunnel creation, major bleeding occurred in 8 (7%) patients, and 6 (5.7%) patients suffered pneumothorax immediate after procedure. All the complications were managed conservatively. During a mean follow-up period of 25 months (range 6–59.4 months), treatment success was achieved in 106/115 patients (93.5%). Mean LES pressure was 54.5 mmHg (28.5–81.4) and 16.4 mmHg (4.8–25.3) before and after the procedure ($P < 0.05$), respectively. Mean Eckardt score was 6.2 (3–11, median 6) and 0.5 (0–2, median 1) before and after POEM, respectively ($P < 0.05$). 20 patient (17.3%) developed mild reflux symptoms and required

**P1215**

| Hb value Before transfusion | | | | Hb value After transfusion | | | Mortality according to Hb value after | |
|---|---|---|---|---|---|---|---|---|
| **Hb** | **Patients** | **Frequency** | **Transfusions** | **Hb** | **Pts nr.** | **Frequency** | **Death** | **Frequency** |
| gr. /dL | N. | % | Mean Units (S.D.) | gr. /dL | N. | % | N. | % |
| **<=7** | 688 | 43.1 | 3.8 (2.1) | **<=7** | 17 | 1.1 | 11 | 64.7 |
| **7–8** | 396 | 75.6 | 2.5 (1.5) | **7–8** | 76 | 5.8 | 11 | 14.5 |
| **8–9** | 264 | 92.2 | 2.7 (1.9) | **8–9** | 415 | 31.8 | 34 | 8.2 |
| **9–10** | 78 | 97.1 | 2.7 (2.6) | **9–10** | 581 | 68.2 | 32 | 5.5 |
| **>=10** | 47 | 100 | 2.5 (1.7) | **>=10** | 508 | 100 | 36 | 7.1 |

intermittent medication with proton pump inhibitors during the follow-up.
**Conclusion:** Our study demonstrated that POEM is a safe, and effective treatment for achalasia. Further studies are warranted to evaluate the long-term efficacy and to compare POEM with other treatment modalities.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1217 PERORAL ENDOSCOPIC MYOTOMY IS SAFE AND EFFECTIVE FOR ACHALASIA IN PATIENTS OLDER THAN 60 YEARS OF AGE COMPARED WITH YOUNGER PATIENTS

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**Introduction:** Peroral endoscopic myotomy (POEM) has been proved to be effective for treating achalasia, but there are limited data on POEM in the elderly patients.
**Aims & Methods:** This study was aimed to assess the role of POEM for achalasia in patients 60 years of age and older. All consecutive patients underwent POEM between December 2011 and Novermber 2015 at a single center were retrospectively reviewed. Patients with age $\geq$ 60 years old were assigned to group A, while patients younger than 60 years old were assigned to group B. Demographic, clinical, manometric data, treatment outcomes and adverse events were compared between these groups.
**Results:** During the study period, one hundred and seven patients (15 in group A, and 92 in group B) were enrolled. The mean age of the group A was $63 \pm 8$ years (range 60–72; 53% female) and that for the group B was $45 \pm 7.6$ years (range 18–58; 56% female). There were no significant differences in the sex and other baseline characteristics between the two groups. Procedural time in the group A was similar to the group B ($54.8 \pm 24.9$ vs. $52.0 \pm 20.7$ min, $P > 0.01$). There was also no significant difference in the incidence of intraoperative complications ($P > 0.01$) and gastroesophageal reflux rate (21.2% vs. 23.5%, $P > 0.01$) between the two groups. During the mean follow-up period of 23 months, treatment success (Eckardt score $\leq 3$) was achieved in 93.3% (14/15) of patients in group A and 92.3% (85/92) of patients in group B ($P > 0.01$).
**Conclusion:** POEM can safely be performed in elderly patients, providing significant symptom relief. POEM may be recommended as the first therapeutic approach to achalasia in elderly achalasia patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1218 TRANSORAL OUTLET REDUCTION FOR THERAPY OF WEIGHT REGAIN AFTER GASTRIC BYPASS

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**Introduction:** Enlargement of gastrojejunal anastomosis aperture is associated with weight regain in patients with Roux-en-Y gastric bypass (RYGB) 1. Endoscopic transoral outlet reduction (TORe) has proven safe and effective for treatment of weight regain. The objective of this study was to evaluate the results of endoscopic outlet reduction in single Italian center.
**Aims & Methods:** The series included consecutive post-RYGB patients with weight regain and enlarged gastrojejunal anastomosis aperture (>15 mm). Endoscopic reduction was performed with Overstitch (Apollo Endosurgery) which is a full-thickness endoscopic suturing device. All the procedures were done at the Digestive Endoscopy Unit of the Catholic University of Rome.
**Results:** Twenty-two patients who had weight regained after RYGB (BMI > 30) underwent TORe from January to December 2015. Baseline mean BMI was 36.8 (range 33–43.6) and weight was 104.5 kg (range 85–131). The procedure was done with the Overstitch and Olympus double channel operative endoscope. An Overtube was placed before the procedure in all patients. Before suturing the outlet rims were cauterized with pulsed pulsed Argon Plasma on 40 Watts in all patients. Mean procedure time was 35 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 new redone outlet was tested with standard gastroscope. There were three (13.6%) complications of which two were mild (1 intraoperative bleeding that arrested spontaneously and 1 patient with fever due to small retrogastric collection treated with antibiotics), while one patient (5.2%) had gastric perforation that required urgent laparoscopic surgery. Mean hospital stay was 2.8 days (range 2–10). Telephonic follow-up was done at 1, 3 and 6 months. Mean BMI at 1 month follow-up was 33.8, at 3 months was 32.4 while at 6 months was 32.3.
**Conclusion:** In our experience TORe was safe and effective procedure in patients with weight regain after RYGB. Longer follow-up and larger clinical trials are needed to establish the durability of these results and to better understand the role of TORe after RYGB and the methods for proper selection of the patients.
**Disclosure of Interest:** I. Boskoski: Dr. Ivo Boskoski is consultant for apollo endosurgery
All other authors have declared no conflicts of interest.

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## P1219 A NEW THERAPEUTIC LASER SYSTEM FOR ADVANCED ENDOSCOPIC TREATMENTS IN THE UPPER GI – FIRST RESULTS IN AN ESTABLISHED ANIMAL MODEL

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**Introduction:** The Thulium laser system is a novel therapeutic technique for open surgery and endourological treatments [1]. Recent experience on animal models showed that the wavelength of 2$\mu$m allows for ablation and vaporesection of the superficial GI layer providing efective control on penetration depth (0.2–0.4 mm) and tissue damage [2].
**Aims & Methods:** We conducted a pilot study in an established animal model to test both feasibility and safety of the Thulium Laser system (Cyber TM®, Quanta System, Varese, Italy) for gastric endoscopic submucosal dissection (ESD) and endoscopic ablation of esophageal lesions. For gastric ESD, different optical fibers (272 and 365 um thick) were evaluated with various power settings (15, 20, 25, 30, and 35 watts) and laser configurations (continued or pulsed modality). The ESD of large (>3 cm) injection-induced lesions of the stomach was performed following a standard technique. For safety, we evaluated the depth of laser ESD impact on gastric layers after having completed the resection. For ablation of artificial esophageal lesions, we used a dedicated 600um side fiber with a line beam that emerges at 45 degrees with soft power settings (5–10 watts) and continued laser modality. The safety endpoint was the lateral and vertical spread of tissue damage induced by laser ablation after having vaporesected circumpherentially a 3 cm-length esophageal surface. All procedures were performed using standard HD video-gastroscope and digitally recorded. Two expert GI pathologists performed histopathological analysis.
**Results:** Neither transmural perforation, nor any muscular layer damage was observed after gastric ESD procedures. Both fiber diameters and configuration modalities were effective and precise. Complete ESD resection was feasible in all cases in 30–70 minutes, showing a fast learning curve. In esophagus, neither transmural perforation, nor any submucosal layer damage was observed. Each of two endoscopists completed a circumferential ablation of a 3 cm-length esophageal surface in 1 minute. Overall, each laser ablation on target produced mucosal vaporesection with only a diminutive lateral spreading of epithelial injury (1–3 mm), depending on the distance between the fiber's tip and the esophageal target.
**Conclusion:** The Thulium laser system appears to be an effective tool for advanced endoscopic treatments in the upper GI endoscopy. This novel therapeutic technique has proven to be precise and very easy to use for gastric ESD and esophageal ablation in ex vivo animal models, thereby showing promising results concerning its safety. In vivo studies should now confirm these initial results in a prospective, multicenter setting.
**Disclosure of Interest:** F. Fagnani: Filippo Fagnani is currently employed at Quanta System S.p.A.
All other authors have declared no conflicts of interest.

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## P1220 THE IMPORTANCE OF GASTROSCOPY BEFOR BARIATRIC SURGERY, ITS IMPACT ON THE SURGICAL PROCEDURE AND FOLLOW-UP COMPLICATIONS

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**Introduction:** The prevalence of obesity is increasing worldwide. Bariatric surgery has increased dramatically in the last few decades. A variety of upper gastrointestinal abnormalities have been noted in obese patients. Pre-operative

multidisciplinary evaluation is recommended. The role of pre-operative upper endoscopy is still controversial.
**Aims & Methods:** To evaluate the role of gastroscopy in the obese population before bariatric surgery and its impact on the per-procedural outcomes. Six hundred and twenty-eight adult patients who underwent bariatric surgery (sleeve gastrectomy or RYGB), from 3/ 2007 to 3/2015, in our hospital were included. Patient's data such as demographics, BMI, comorbidities, medications, gastroscopy findings, barium swallow studies, biopsy, HP status, surgery, peri-procedural complications, resected stomach pathology, imaging reports and laboratory parameters were reviewed retrospectively. The patients were divided in 2 groups, Group A (barium imaging before surgery) and Group B (gastroscopy before surgery). Comparison was made between the 2 groups.
**Results:** Groups A and B consisted of 442 and 188 patients, respectively. Group B (gastroscopy) patients were older than group A (barium swallow) (mean age 45 Vs 39.7), had more previous bariatric surgeries (17.2% vs.7.2%) and received more anti platelet and anticoagulation medications (30.1% vs. 16.7%) ($p < 0.01$). Two patients in group B (gastroscopy) (2/188, 1.06%) had significant findings that precluded surgery. No statistically significant difference was found between the two groups in terms of the findings in the pre- procedural imaging, the type of operation preformed, additional procedures in surgery, macroscopic abdominal findings at the time of surgery, histopathological findings, HP status, surgical complications and the average decrease in BMI. In 99% of patients, pre surgical endoscopic findings were not significant and included mainly mild peptic lesions and gastric polyps (all polyps non-neoplastic, requiring to treatment). In both groups, a significant improvement in BMI and laboratory parameters such as liver enzymes, cholesterol, triglycerides and HBA1C was demonstrated post-surgery.
**Conclusion:** Pre procedural gastroscopy rarely offers advantage before bariatric surgery. It is costly and time consuming but significant pathology can be found and therefore should be considered routinely before bariatric surgery.
**Disclosure of Interest:** F. Benjaminov: I am the author and presentor
D. Feldman: Work in same hospital
A. Stein: Co workers
F. Konikoff: head of departement
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## P1221 PERORAL ENDOSCOPIC SHORTER VERSUS LONGER MYOTOMY FOR THE TREATMENT OF ACHALASIA: A COMPARATIVE STUDY

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**Introduction:** Presently, peroral endoscopic myotomy (POEM) has been developed to treat esophageal achalasia as a less invasive mode. It allows for cutting the esophageal and proximal circular muscle bundle by creation of a submucosal tunnel.
**Aims & Methods:** We aimed to compare clinical efficacy and safety between peroral endoscopic shorter and longer myotomy for treating achalasia. Between July 2011 and September 2015, 38 patients underwent peroral endoscopic shorter myotomy (myotomy length $\leq$ 7 cm) in our department. These patients were matched by age, gender, symptoms duration, Eckardt score, and LES pressure with 59 patients who underwent longer myotomy (myotomy length $>$ 7 cm). Procedure-related parameters, manometry outcomes and complications were compared between the two groups.
**Results:** There was no significant differences in baseline characteristics between the two groups. Mean myotomy length was $6.1 \pm 0.5$ cm in shorter myotomy group, and $11.7 \pm 2.4$ cm in longer myotomy group ($P = 0.000$). The mean operation time was significantly less in shorter myotomy group than longer myotomy group ($44.2 \pm 16.3$ min vs. $68.5 \pm 23.2$ min, $P < 0.01$). During a median follow-up period of 24 months (range 7–38.2 months), treatment success (Eckardt score $\leq$ 3) was achieved in 92.1% (35/38) of patients in shorter myotomy group and 91.5% (54/59) of patients in longer myotomy group ($P > 0.01$). There was also no statistical difference in the incidence of intraoperative complications (7.4% vs. 9.2%, $P > 0.01$) and gastroesophageal reflux diseases (17.2% vs. 18.5%, $P > 0.01$) between the two groups.
**Conclusion:** POEM was effective and safe for treating achalasia, and shorter myotomy is comparable with longer myotomy for treating achalasia with regard to long-term clinical efficacy and safety, and have the advantage of shorter procedure time. Further randomized controlled trials are warranted to evaluate the efficacy and safety of these two myotomy methods.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1222 NOVEL DEVICE FOR FULL THICKNESS ENDOSCOPIC SUTURE, USING BACK AND FORTH NEEDLING: EX VIVO ANIMAL STUDY

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**Introduction:** Nonsurgical endoscopic closure of the gastrointestinal wall may be desired in many situations, such as fistulae, perforation. With the emerging and development of natural orifice transluminal endoscopic surgery (NOTES) as a minimally invasive surgical platform, endoscopic suturing is especially important. Here, we studied the feasibility of new developed endoscopic suturing device by demonstrating the strength of closure in ex vivo animal study.
**Aims & Methods:** A total of 30 porcine stomachs were used for the test. Standard gastrotomy was made on each stomach by blade incision. Porcine stomachs were assigned randomly to 3 groups and closed by new endoscopic closer with curved needle (En-closer), endoscopic clips and hand sewn. Each stomach was inflated by an automated pressure gauge. After that, the stomach was dipped in water and air leakage pressure was measured by automated pressure gauge when an air bubble was first observed.
**Results:** The average leakage pressure for the En-closer, Endoclip, and full-thickness hand sutures was 43.25 mmHg, 44.10 mmHg, and 63.19 mmHg. The average closer strength of the En-closer does not significantly differ from that of the Endoclip ($p > 0.05$). The standard deviation for the En-closer, Endoclip, and full-thickness hand sutures was 6.37 mmHg, 14.35 mmHg, and 12.97 mmHg, respectively. The standard deviation of the En-closer is significantly smaller than that of the Endoclip and full-thickness hand sutures ($P < 0.05$). It is determined that the closer strength of the En-closer does not significantly differ, but is more consistent than the closer strength of the Endoclip.
**Conclusion:** The En-closer, which can performs multiple stitches with a single endoscope insertion showed feasible result comparing with Endoclip and hand-sewn suture. This research proposes a novel approach for minimally invasive endoscopic surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1223 NEWLY DESIGNED HIGHLY FLEXIBLE MAGNETIC DEVICE FOR ENDOSCOPY ASSISTED FERROMAGNETIC FOREIGN BODY REMOVAL

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**Introduction:** Metallic foreign bodies have been removed under endoscopic guidance. Removal of sharp objects using an overtube or hood has been reported, It can be hazardous. There are reports of magnetic devices which are less flexible, with plastic sheath and thick metal wire. We have designed a newer device.
**Aims & Methods:** To evaluate our experience with newly designed highly flexible magnetic device for endoscopy guided Ferromagnetic foreign body removal Patients presenting with history of metallic foreign body ingestion included. X ray abdomen done. Informed consent taken. We used nitinol hydrophilic guide wire (200 cm in length, 0.035 inch thick) with two 6-mm-diameter magnetic discs (with a strength of 0.18 tesla) fixed at the base of 10 cm long hydrophilic tip. A ligator cylinder was used during foreign-body retrieval (Figure [1]). The cylinder was fixed at the tip of the endoscope. Guide wire passed in the channel through the tip of the endoscope, So that the magnet was positioned at the tip of the endoscope. As the endoscope reached the foreign body, the magnet was pushed out and the foreign body stuck to the magnet. Part of foreign body and magnet were then drawn into the cylinder and the endoscope was removed. Pentazocine (15 mg) and hyosine butylbromide (20 mg) were used as premedication. The time required, and the complication and failure rates were recorded.
**Results:** Ten patients 9 children (1 to 10 years old), one 18 years old female, who had ingested sharp and rounded foreign bodies were included in the study. 5 cases ingested large coin, 1 had ingested pin, 1 had ingested safety pin, 1 ingested key, 1 child had ingested earring, 1 ingested screw, no foreign body was impacted and none penetrating. 9 foreign bodies were in stomach, while key just beyond DJ flexure. All the foreign bodies were removed using this method without any complications in mean time of 57 seconds (range 40–126 seconds). We first time used our instrument for coins (figure 2), later for sharp metals. We could use our retriever for gastric foreign body even in nonfasting patient. Key reached beyond DJ flexure, we pushed the magnetic retriever beyond DJ flexure, took out the key. In duodenum and proximal jejunam where placing the scope is difficult, using the endoscopic accessories like snare and rat-tooth forceps not possible this

device can be used. This new retriever which is more flexible because of use of nitinol guidewire, and the magnet is small and strong, it can get stuck to foreign body in food material, it can reach up to proximal jejunum to takeout foreign body. The sharp foreign bodies were light and so were attracted by the small magnet, and the pulling back of the magnet led to their disimpaction. We have not used it for penetrating sharp foreign bodies, possible they can also be pulled out because the head portion of the pins and safety pins can be visualized. The portion of the foreign body with a larger surface area had a tendency to stick to the magnet, and tend to aligned themselves along their longitudinal axis. The sharp end of the foreign body followed the head, thus avoiding mucosal injury. This device is safe for use even in small kids, no risk of injury to endoscope and Gastrointestinal wall, no need of sheath to cover the wire. Size of magnet is small so it can easily cross Narrow areas of upper GIT.
**Conclusion:** New magnetic device is highly flexible, easy to use, with no risk of injury to patient and scope, effective even for proximal jejunum ferromagnetic foreign body removal.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1224 CLINICAL OUTCOMES IN VERY ELDERLY PATIENTS WITH GASTRIC CANCER TREATED USING ENDOSCOPIC SUBMUCOSAL DISSECTION: ANALYSIS WITH EMPHASIS ON THE RELATIONSHIP BETWEEN PATIENT CHARACTERISTICS AND PROGNOSIS


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**Introduction:** With an increase in the aging population, there are increasing chances of encountering very elderly patients with early gastric cancers (EGCs). Now endoscopic submucosal dissection (ESD), which has been widely accepted as a less invasive treatment option for EGC compared with surgery, is increasingly performed for the very elderly patients. However, only limited data are available regarding gastric ESD in this population. Furthermore, the prognosis of very elderly patients with EGC treated using ESD and the associated prognostic factors have rarely been examined, although these are essential in determining the significance of treatment with ESD in this population.
**Aims & Methods:** Here, we aimed to examine the clinical outcomes and prognosis in very elderly patients with EGC treated using ESD and to identify the associated prognostic factors. We retrospectively reviewed 108 elderly patients aged≥ 85 years with 149 EGC lesions treated using ESD between January 1999 and December 2014 at our institution. The evaluated outcomes included en bloc/R0/curative resections, complications, procedure time, and overall survival (OS). To identify the prognostic factors, the relationships between OS and the following factors were assessed by univariate analysis using log rank tests and multivariate analysis using a Cox proportional hazard model: ESD curability, sex, performance status (PS), Charlson comorbidity index (CCI),[1] Onodera's prognostic nutritional index [PNI, calculated using the following formula: 10 × serum albumin value (g/dl) + 0.005 × total lymphocyte count (per $mm^3$) ],[2,3] the neutrophil-to-lymphocyte ratio (NLR),[4] and the modified Glasgow prognostic score (mGPS).[5]
**Results:** The patients included 82 males and 26 females, with a median age of 86 years (range: 85–93 years). PS according to the Eastern Cooperative Oncology Group (ECOG) scale was 0–1 for all patients, and PS according to the American Society of Anesthesiologists was 2 in 89 patients and 3 in 19 patients. CCI varied between 0 and 5, and 94 patients (87.0%) showed an index of 1 or higher. In the majority of patients (92.6%), mGPS was 0. The median value of PNI was 48.9 (range: 31.4–59.1), and the median NLR was 2.2 (range: 0.6–7.3). En bloc, R0, and curative resections were achieved in 98.0%, 91.3%, and 72.7% lesions, respectively, with a median procedure time of 60 min. Regarding complications, perforation and delayed bleeding were observed in 0.7% and 5.4% lesions, respectively. There were no severe complications that required surgery and no treatment-related deaths. Following ESD, 23 deaths, including two deaths due to gastric cancer, were observed during the median follow-up period of 40.2 months (range: 1.8–108.7 months); the 3- and 5-year OS rates were 90.3% and 72.0%, respectively. Univariate analysis showed that PNI was the only factor significantly associated with OS; the 3- (54.3% vs. 95.9%) and 5- (54.3% vs. 76.3%) year OS rates were significantly lower in patients with low PNI (< 44.6; the cutoff value was determined using the receiver operating characteristic analysis) than higher PNI ($P < 0.001$). In addition, multivariate analysis showed that low PNI (< 44.6) was the only independent risk factor for poor OS (HR, 5.5; 95% CI, 1.9–15.8; $P = 0.002$).
**Conclusion:** The present study clarified the feasibility and safety of ESD for elderly EGC patients aged≥ 85 years with ECOG-PS between 0 and 1. The finding that a relatively large proportion of the elderly patients treated using ESD were estimated to live longer than 5 years also supports the validity of ESD for this population. However, patients with low PNI were found to be at higher risk of poor prognosis, indicating the need to evaluate PNI in determining whether to perform ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1225 THE EFFECT OF A FLEXIBLE 3D ENDOSCOPE ON THE LEARNING CURVE OF ENDOSCOPIC SUBMUCOSAL DISSECTION: A BENCH TOP EX-VIVO STUDY


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**Introduction:** Endoscopic submucosal dissection (ESD) is a technically challenging procedure with a steep learning curve. The lack of depth perception from a conventional 2D endoscope may be a contributing factor to its difficulty. This study assesses the effect of a 3D flexible endoscope on the learning curve of gastric ESD.
**Aims & Methods:** This is a prospective preclinical bench study to compare the effect of 3D endoscope on the performance of ESD between an experienced endoscopist and a novice. The participants included an endoscopist with more than 1000 endoscopic procedures but little experience in ESD and a novice with total endoscopic experience of less than 50 cases. The performance of gastric ESD was standardized in an ex-vivo porcine model using a prototype 3D endoscope (Olympus R&D, Tokyo, Japan). Each participant was asked to perform 8 ESD over the greater curvature using Dual knife jet (Olympus Co Ltd). The time to complete ESD, occurrence of perforation and en-bloc resection rate were recorded. Resected specimens were digitalized and surface area was calculated using GIMP 2.8 image analysis software. Descriptive statistics and non-parametric analysis was performed using IBM SPSS v22.
**Results:** En bloc resection was achieved in all ESD procedures without perforation. The median resected area by the experienced endoscopist was $3.8cm^2$ (min: $1.04cm^2$ max: $7.9cm^2$), which showed no significant difference from that achieved by the novice endoscopist with the median area of 3.3 $cm^2$ (min: $0.86cm^2$ max: $8.25cm^2$) ($p = 0.87$). The median operative time corrected for surface area resected for the experienced endoscopist was 197.9 $s/cm^2$ (min: 60.9 $s/cm^2$ max: 1897.4 $s/cm^2$), which was significantly lower than that of the novice endoscopist (median resection speed = 434.7 $s/cm^2$ (min: 217.2 $s/cm^2$ max: 1544.2 $s/cm^2$)) ($p = 0.05$). For both participants, resection speed plateaued after the third ESD procedure. The learning curve can be summarize by the equation $y = 1183.4x^{-0.807}$ ($R^2 = 0.6927$).

| Trial | Experienced ($s/cm^2$) | Novice ($s/cm^2$) |
|---|---|---|
| 1 | 1897.4 | 1544.2 |
| 2 | 1066.1 | 332.2 |
| 3 | 236.0 | 337.5 |
| 4 | 201.1 | 358.0 |
| 5 | 194.8 | 217.2 |
| 6 | 74.8 | 679.8 |
| 7 | 119.1 | 568.6 |
| 8 | 60.9 | 511.4 |

**Conclusion:** This preclinical bench study illustrated that the use of prototype 3D endoscope may shorten the learning curve for ESD. 3D images improved depth perception for the endoscopist and resulted in better en-bloc resection as well as preventing perforation. This will especially be useful for low experience endoscopists to master ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**P1226 Table 1:** Diagnostic accuracy of T-staging by CE or EUS (top) and subgroup analysis by CE diagnosis followed by EUS (bottom).

| | CE | | | EUS | | |
|---|---|---|---|---|---|---|
| **Histology** | M/SM1 | SM2 or deeper | Inconclusive | M/SM1 | SM2 or deeper | Inconclusive |
| **M/SM1** | 117 | 9 | 0 | 110 | 16 | 0 |
| **SM2 or deeper** | 21 | 8 | 1 | 9 | 20 | 1 |
| **Total accuracy** | 80.1% | | | 83.3% | | |
| **CE** | M/SM1 | | | SM2 or deeper | | Inconclusive |
| **EUS** | M/SM1 | SM2 or deeper | Inconclusive | M/SM1 | SM2 or deeper | SM2 |
| **Histology** | | | | | | |
| **M/SM1** | 103 | 14 | 0 | 7 | 2 | 0 |
| **SM2 or deeper** | 8 | 12 | 1 | 1 | 7 | 1 |

CE, conventional endoscopy; EUS, endoscopic ultrasonography; M/SM1, mucosal cancer or cancer in the submucosa $<500\mu$m from the musculairs mucosae; SM2, cancer in the submucosa $\geq 500\mu$m from muscularis mucosae.

## P1226 PRACTICAL STRATEGY FOR INVASION DEPTH PREDICTION OF EARLY GASTRIC CANCER BY CONVENTIONAL ENDOSCOPY AND ENDOSCOPIC ULTRASONOGRAPHY

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**Introduction:** Conventional endoscopy (CE) and endoscopic ultrasonography (EUS) are useful approaches for predicting the depth of invasion in early gastric cancer (EGC), but the diagnostic accuracy were unsatisfatory.

**Aims & Methods:** This study aimed to propose an effective strategy by combining CE and EUS for therapuetic decision.

**Methods:** A total of 150 patients (156 lesions) with superficial gastric cancers underwent both CE and EUS before therapy at Peking Union Medical College Hospital from January 2006 to December 2015. All the lesions were resected either endoscopically (n = 98) or surgically (n = 58), and divided into two histologic groups: superficial invasion referred cancers that limited in mucosal layer or less than 500$\mu$m into the submucosal layer (m/sm1, n = 126) and deep invasion referred those which were more than 500$\mu$m into the submucosal layer or deeper ($sm^2$ or deeper, n = 30). Endoscopic images of CE were reviewed by one experienced endoscopist who was blind to the clinical information, and invasion depth were predicted. The EUS-based tumor depth was reported according to the EUS records, which combined the endoscopic features and ultrasonographic images in practice. Diagnostic accuracy of each method was compared with the histology of the resected specimen. And impact factors for diagnosis were investigated.

**Results:** The overall accuracy rates in invasion depth of superficial gastric cancer were 80.1% for CE and 83.3% for real EUS respectively (P = 0.73). But in the subgroup with more observer confidence, diagnostic accuracy of CE was significant higher than that with unconfidence (92.1% vs. 72.0%, $P < 0.01$). Impact factors associated with CE mis-staging included: unclear images (OR = 418.4, $P < 0.01$), remarkable redness of lesions (OR = 16.2, P = 0.01), histological $sm^2$ or deeper invasion (OR = 1830.7, $P < 0.01$) and undifferentiated carcinoma (OR = 60.7, P = 0.01). Nine of 17 lesions (52.9%) were over-staged by CE, which were expected as surgical candidates. 41.2% of the over-staging lesions avoided surgery by additional EUS assessment.

**Conclusion:** Both CE and EUS are useful for T-staging of superficial gastric cancers. Observer confidence is associated with higher accuracy of CE. Sequential EUS may avoid overtreatment for the lesions with superficial invasion.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1227 EVALUATION OF ENDOSCOPIC TREATMENT FOR SUPERFICIAL DUODENAL NEOPLASM

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**Introduction:** Superficial duodenal neoplasm is a rare disease. Recently, the improvement of endoscopic technologies has been suggested to lead to better recognition of duodenal adenoma and early cancer. Duodenal ESD has not been standardized because of difficulty and a very high risk of complications. However, the surgical treatment loads a large burden and functional disorder may remain depending on the location. Thus, minimally invasive treatment is needed.

**Aims & Methods:** In this study, the outcomes of 183 duodenal tumors treated at our hospital between July 2010 and February 2016 were investigated, and the safety and efficacy of EMR and ESD were evaluated.

**Results:** The subjects were patients at a mean age of 62.4 years old (29–85), and the sex ratio (male/female) was 115/56. The location of the lesion was bulb in 24, SDA in 19, descending part in 124, LDA in 10, and horizontal part in 6, circumferentiality was <1/2 in 163 and >1/2 in 20, and the macroscopic type was elevated in 141 and depressed in 42. The treatment method employed was EMR in 62, ESD in 106, circumferential EMR in 5, EMRL in 3, and resection by forceps in 5. The mean tumor diameter was 18.3 mm (2–60), and the lesion was adenoma in 126, cancer in 47, carcinoid in 6, and others in 4. The cancer-bearing rates exceed with the tumor size. By the procedure, in 62 lesions treated with EMR (excluding large Brunner gland adenoma in the bulb treated with planned piecemeal resection), the mean tumor diameter was 9.1 mm (2.5–21), and the lesion was adenoma in 56, adenocarcinoma in 3, carcinoid in 1, and another in 2. The en bloc resection rate was 95% (59/62), and the complete en bloc resection rate was 75% (47/62). No complication occurred (delayed bleeding: 0, perforation: 0). In the 106 lesions treated with ESD, the mean tumor diameter was 24.6 mm (2–75) and mean procedure time was 77.5 minutes (10–360). The lesion was adenoma in 60, adenocarcinoma in 43, carcinoid in 2, and another in 1. The en bloc resection rate was 97% (103/106), and the complete en bloc resection rate was 81% (82/106). Regarding complications, delayed bleeding and perforation occurred in 9 (8%) and 13 (13%), respectively. All delayed bleeding cases were conservatively treated by endoscopic hemostasis. Perforation required surgical treatment in 2 (2%).

**Conclusion:** This study clarified that the cancer-bearing rate of duodenal tumors rises with an increase in the diameter. For small lesions, EMR with a simple procedure causing fewer complications may be sufficient, but reliable resection is needed for the treatment of large lesions. Although duodenal ESD is very difficult with a high risk, when it is performed by experienced experts at advanced high-volume centers, it may be minimally invasive treatment for which marked efficacy while retaining safety can be expected.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1228 CREATION OF GASTROINTESTINAL SUBMUCOSAL TUNNEL UPON SUBMUCOSAL INJECTION OF A PLGA-PEG-PLGA THERMOGEL IN A PORCINE MODEL: THE NEXT GENERATION OF TUNNEL ENDOSCOPY? (WITH VIDEO)

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**Introduction:** Tunnel endoscopy is an innovative endoscopic technique which plays a crucial role in multiple endoscopic interventions. The creation of a gastrointestinal submucosal tunnel is, however, still technically challenging and time consuming, which significantly limits its clinical applications.

**Aims & Methods:** To evaluate the use of a biocompatible and biodegradable poly (lactic acid-co-glycolic acid)-poly (ethylene glycol)-poly (lactic acid-co-glycolic acid) (PLGA-PEG-PLGA) thermogel (a physical hydrogel formed simply by body heating after injection) as the submucosal injection agent for facilitating the establishment of a submucosal tunnel in esophagus, stomach, and colon.

**Results:** Submucosal tunnels were established successfully in all three sites for all three minipigs without any complications. The PLGA-PEG-PLGA aqueous solution was easily injected into colonic submucosa and then transformed into a semi-solid gel due to contacting with warmer surroundings, resulting in the formation of a thick submucosal cushion. The cap-fitted endoscope was introduced into submucosal space and moved forward gradually by suctioning the in situ-formed thermogel until the tunnel was completed. There was no need for additional electrocautery or blunt dissection. Neither bleeding nor perforation occurred. The median procedure time was only 13.6 mins, 11.5 mins, and 9.6 mins, respectively.

**Conclusion:** Our experiments confirmed that PLGA-PEG-PLGA thermogel was suitable as a submucosal injection substance to establish tunnels safely, conveniently, and rapidly in digestive tract, and had a significant advantage by conducting submucosal auto-dissection in the cushion along the inherent anatomical layer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1229 IS THERE A PLACE FOR BALLOON DILATATION IN THE ERA OF PERORAL ENDOSCOPIC MYOTOMY IN PATIENTS WITH ACHALASIA?

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**Introduction:** In patients with achalasia, peroral endoscopic myotomy (POEM) is now the proposed method to replace other endoscopic treatments, having a low morbidity and similar or even higher efficacy than its surgical counterpart, the Heller myotomy. However, balloon dilatation is still performed by many.

**Aims & Methods:** The aim of the present study was to test the effectiveness, the outcome at one year and complications of POEM in consecutive patients with symptomatic achalasia in comparison with pneumatic balloon dilatation. All patients who presented with symptomatic achalasia were treated with either pneumatic dilatation or POEM, depending on the age, comorbidities, previous esophageal surgery or patient's wish. Symptoms were assessed using the Eckardt score (0–12). Endoscopic and radiological assessments were performed in all patients before treatment and at 1 month after treatment. In patients undergoing POEM, a manometry was also carried out before and 1 month after treatment. The patients were regularly contacted for follow-up at 1, 6 and 12 months after treatment. Patients with failure of the initial procedure were treated again, depending on the initial response and the patient's wish.

**Results:** From November 2013 to May 2015, 46 consecutive patients were treated with either POEM (n = 35) or pneumatic dilatation (n = 11). No patient had previous surgical myotomy in the POEM groups, while 4 patients had previous Heller myotomy in the dilatation group. There were significant improvements in the Eckardt scores of all patients treated, in both the POEM group (before 7.8, after 0.8) and the dilatation group (before 7.5, after 1.7). We recorded 5 incidents in the POEM group, 3 esogastric microperforations, closed safely with endoscopic clips, 1 subcutaneous emphysema, for which temporary cessation of the intervention was necessary, and 1 pneumoperitoneum, for which transumbilical decompression using a Veres, needle was necessary. We also recorded 2 complications in the form of postprocedural endoscopic clip slippage, which required endoscopic reintervention. No incidents or complications were noted in the dilatation group. All patients treated with POEM were symptom free at 1, 6 and 12 months after treatment. In the dilatation group, 3 patients relapsed at 3 months after treatment, needing additional dilatation. The 8 other patients remained symptom free at 6 and 12 months. There were no statistical significant differences ($p = 0.083$) with regard to overall treatment failure and outcome at one year between patients treated with POEM and those with balloon dilatation.

**Conclusion:** POEM is an efficacious method for treating achalasia but requires an expert endoscopist with special training. Even in centers where POEM is the standard of care, selected cases could benefit from balloon dilatation, with a similar medium-term efficacy to POEM.

## P1230 A SIMPLE MATHEMATICAL EQUATION FOR RELIABLE PREDICTION OF THE GASTRO-ESOPHAGEAL JUNCTION THROUGH THE SUB MUCOSAL TUNNEL DURING PER ORAL ENDOSCOPIC MYOTOMY – A PROOF OF CONCEPT PILOT STUDY

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**Introduction:** Per oral endoscopic myotomy (POEM) is an accepted treatment for achalasia cardia (AC). Accurate estimation of distance to gastro-esophageal junction (GEJ) through the tunnel is often a technical challenge during POEM. Currently employed methods have limited accuracy. Tunneling is often performed by periodically alternating between tunnel and lumen to ensure extension up to and beyond GEJ. An error at this step may lead to an incomplete myotomy; and procedure time may be prolonged. We have observed that distance to GEJ measured through the tunnel is longer than when measured through the esophageal lumen.

**Aims & Methods:** Our hypothesis states that additional distance when traversing the tunnel is directly proportional to the esophageal diameter; and can be calculated by an equation $X = Y + CZ$ (X = GEJ distance through tunnel, Y = GEJ distance through lumen, Z = max. esophageal diameter & C = arithmetic constant). If a reliable C is derived, estimation of GEJ distance during POEM may be possible. This study evaluates accuracy of this hypothesis & the calculated C constant. Patients & methods: Total N = 22: Gr. I – 12 retrospective patients who had undergone POEM; Gr. II – 10 prospective patients undergoing POEM. A single operator performed all POEM procedures. Distance to GEJ (Y) was recorded during screening EGD. Max. esophageal diameter (Z) was measured on Barium swallow / CT scan. In Gr. I, GEJ distance through tunnel was measured and recorded during POEM (X). Using formula $C = (X - Y)/Z$, C was calculated. Mean C +/- 2 SD was calculated for Gr. I. This mean C was substituted in equation $X = Y + CZ$ to predict GEJ distance through tunnel (X1) in Gr. II. Y and Z were calculated as in Gr. I. X1 was predicted pre POEM and values were blinded from operator. During POEM, operator recorded true X (X2). X1 & X2 values were compared.

**Results:** POEM was successfully performed in all. Group I (n = 12, 4 – sigmoid) – mean values (range) for X, Y and Z were 42.58 cm (38 – 47), 39.83 cm (36 –45) and 4.39 cm (2.78 – 6.25) respectively. Mean C (Gr. I data) = 0.63 (SD +/- 0.11). Group II (10 patients, 2 – sigmoid) –mean Y = 40.3 cm (36 – 43), mean Z = 6.19 cm (3.75 – 9.62). Mean estimated X1 = 44.199 (40.49 – 48.06), true X2 = 44 cm (41 – 48). X1 and X2 values showed excellent correlation (Correlation coefficient = 0.991, $p < 0.01$).

**Conclusion:** Disparity in distance to GEJ through lumen and through tunnel is seen during POEM and appears to be proportional to the esophageal diameter. This pilot study suggests an excellent correlation between estimated and actual distances, indicating that the hypothesis & calculated constant C = 0.63 shows excellent reliability throughout current dataset. The equation $X = Y + CZ$ can be used to accurately predict GEJ distance during tunneling. Further studies with a larger database are required to confirm this finding.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1231 SAFETY AND EFFICACY OF COLD POLYPECTOMY FOR NONAMPULLARY DUODENAL ADENOMA: A PROSPECTIVE CLINICAL TRIAL

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**Introduction:** Studies have revealed that cold polypectomy (cold forceps polypectomy [CFP] and cold snare polypectomy [CSP]) is an exceptionally safe and effective treatment for colorectal polyps [1, 2]. With regard to the duodenum, the number of nonampullary duodenal endoscopic resections has been gradually increasing [3]. However, duodenal endoscopic resection has a high incidence of complications such as perforation in the endoscopic mucosal resection (EMR) as well as in the endoscopic submucosal dissection (ESD), compared to resection of other parts of the digestive tract. Therefore, relatively safer treatment alternatives such as cold polypectomy should be considered. However, the cases of duodenal cold polypectomy have been unreported. In this prospective study, we aimed to assess the safety and efficacy of nonampullary duodenal cold polypectomy.

**Aims & Methods:** Patients with one or more small nonampullary duodenal adenoma lesions were enrolled in this clinical trial, while those with polyposis syndrome, including familial adenomatous polyposis (FAP); those with coagulation abnormalities; and those receiving antithrombotic drugs were excluded. The study subjects underwent cold polypectomy (CFP or CSP) between March and November 2015, and subsequent upper gastrointestinal endoscopy 3 months after the intervention. The presence of residual tumor was evaluated by conducting endoscopic examination and histopathologic of tissue samples obtained from the cold polypectomy scars. This study was approved by our institutional medical ethics board.

**Results:** A total of 25 lesions in 19 patients were removed using cold polypectomy. Eleven patients (58%) were men and the mean age of the subjects was $62.7 \pm 11.8$ years. The number of lesions was 5, 17, and 3 per lesion location (1st., 2nd., and 3rd. portion), respectively, and 8, 12, 3, and 2 per macroscopic appearance (Is, IIa, IIa + IIc, and IIc), respectively. Nine lesions in 8 patients were resected using CFP, while 16 lesions in 11 patients were resected using CSP. Seven of 9 (77.8%) and 15 of 16 (93.8%) lesions were removed en bloc using CFP and CSP, respectively; other 3 lesions were removed by piecemeal resection in 2 pieces. All specimens resected using both CFP and CSP were successfully retrieved. Histopathologic analysis showed that 22 of 25 lesions (88%) were adenomas; 19 (76%) were low-grade tubular adenoma; and 3 (12%) were high-grade tubular adenomas. The mean size of the adenomatous lesions was $4.0 \pm 1.4$ mm (2–6 mm). Nine of 22 adenomas (41%) were R0 resections; 3 of 9 (33%) and 6 of 13 (46%) were R0 resections using CFP and CSP, respectively. All post-resection ulcers were closed immediately after cold polypectomy by endoscopic clips. Delayed bleeding and intraprocedural/delayed perforation were not observed in any case. In all patients with adenomas, the scars were identified and biopsied at follow-up endoscopy performed 3 months after cold polypectomy. No residual or recurrent tumor was detected morphologically or histopathologically.

**Conclusion:** Cold polypectomy is a safe and effective treatment for small nonampullary duodenal adenomas. A multi-centric long-term follow-up study with a larger sample size should be conducted to confirm the safety and effectiveness of cold polypectomy for nonampullary duodenal adenoma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1232 ENDOSCOPIC DIAGNOSIS FOR ELEVATED EARLY GASTRIC CANCER THAT SHOWED ADENOMA BY BIOPSY BEFORE ESD


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**Introduction:** Endoscopic differential diagnosis of adenoma and well differentiated adenocarcinoma is considered to be difficult on some gastric elevated tumor. On these lesions, Endoscopic findings of magnified narrow band imaging (M-NBI) was reported to be useful for diagnosis of cancer.

**Aims & Methods:** The aim of this study is to clarify retrospectively details of endoscopic diagnosis for elevated gastric tumor that pathological findings of biopsy performed before endoscopic submucosal dissection (ESD) showed adenoma. From January 2006 to March 2015, 50 lesions in 45 patients were treated by ESD for elevated gastric tumor that pathological findings of biopsy before ESD showed adenoma in our institution. We retrospectively confirmed endoscopic findings, and performed differential diagnosis of gastric adenoma and early gastric cancer (EGC). We defined lesions with redness, depression or rough-surfaced mucosa as cancer on white light imaging and irregular microsurface pattern (IMSV) or irregular microvascular pattern (IMVP) as endoscopic findings of EGC on M-NBI. We clarified clinicopathological features, outcomes of ESD and details of endoscopic diagnosis including sensitivity, specificity, accuracy and so on. In addition, we investigated predictive factors for cancer by uni and multivariate analysis.

**Results:** The clinicopathological features and the details of ESD were as follows; male/female:33/12, median age:72y.o.(57–82) median tumor size:14 mm (4–34) adenoma/EGC:9/41. Histologiacal type of EGC was only well differentiated adenocarcinoma. Sensitivity/specificity/accuracy:75.6%/66.7%/74.0% on WLI and 95.1%/77.8%/92.0% on M-NBI. Among 10 cases that we could not diagnosis as cancer on WLI, nine cases were correctly diagnosed on M-NBI. Positive predictive value of endoscopic findings of cancer: redness:89.5%, depression:100%, rough-surfaced mucosa:88.9%, tumor size (>20 mm):79.2%, IMSP:94.4% and IMVP:100%. On multivariate analysis, IMSP and IMVP were significant predictive factor of cancer.

**Conclusion:** Endoscopic diagnosis by M-NBI is considered to be useful for diagnosis of elevated early gastric cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1233 POEMS POTPOURRI: THE ROUTINE X-RAY AND ENDOSCOPY ARE NOT NECESSARY AFTER POEM; ASPIRIN DOES NOT INCREASE THE RISK OF BLEEDING


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**Introduction:** Peroral endoscopic myotomy (POEM) is a promising new endoscopic method for the treatment of achalasia. The role of several pre-, peri- and postprocedural measures which have been implemented in several centers have not been assessed yet. In our center, we do not require the discontinuation of aspirin before POEM. On the first post-operative day (POD 1), we used to perform both upper GI endoscopy and X-ray with water-soluble contrast to exclude POEM-associated adverse events (AEs), such as a leak or mucosal injury; now, patients are checked by X-ray only.

**Aims & Methods:** The aim of this retrospective study was to analyze 1. the risk of bleeding in patients who had been treated with aspirin before POEM, and 2. to assess the value of routine post-operative examinations (X-ray and upper GI endoscopy) which are usually performed on POD 1.

**Results:** A total of 138 POEM procedures have been performed in 134 patients (4 re-POEMs) in our center since 2012 (mean age 46.5). Only one patient experienced a severe AE (pleural effusion) which required prolonged hospitalization (15 days) with drainage; otherwise, we have not experienced any other severe AE and all patients were discharged on POD 1–2 (mean hospital stay was 1.8 days (SD 1.4)). A total of 10 patients were treated with aspirin (or other antiaggregants) prior to POEM; 3 of these patients had aspirin withdrawn before the procedure. Minor bleeding during POEM occurred in 4 patients (3%) and were successfully managed endoscopically; all occurred in patients without aspirin. We did not experience any bleeding after POEM on POD 1, 2 or later. Upper GI endoscopy on POD 1 was done in 79 patients; out of these, 7 had minor findings such as mucosal injury (all resolved spontaneously) and 3 received additional clips at the site of incision. X-ray on POD 1 was done in 134 cases, and a minor leak was present in 4 of these (2.9%) – these patients were left on nil per mouth and all leaks resolved spontaneously.

**Conclusion:** Routine post-POEM X-ray examination and/or upper GI endoscopy in patients with achalasia are probably not warranted because of the negligible rate of clinically relevant findings. Furthermore, the use of aspirin does not seem to increase the risk of peri- or postprocedural bleeding.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1234 MORTALITY CAUSES FROM ACUTE UPPER GASTROINTESTINAL BLEEDING: A PROSPECTIVE MULTICENTRE OBSERVATIONAL STUDY


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**Introduction:** The epidemiology of bleeding from variceal (V) and non-variceal (NV) sources and the risk factors for upper gastrointestinal bleeding has changed over the time. The increased proportion of older patients with different comorbities together with an improved life expectancy modified the risk factors for death by acute upper bleeding.

**Aims & Methods:** We aimed to verify the mortality causes in patients with variceal and non-variceal gastrointestinal sources of bleeding. Data on patients admitted for GI bleeding were collected from Jan 2014 to Jan 2016. Related haemorrhagic death is defined as any death occurred within 30 days from the admission for patients with NV bleeding and within 42 days for those with varices. Mortality due to bleeding episode was defined as any death occurred within 48 hours from the endoscopy.

**Results:** A total of 3224 patients were included. Of these 2,764 (83.1%) had a NV source (mean age 69.1 ± 16.2) and 560 had varices (mean age 63.2 ± 12.3) ($p < 0.000$ for age). Comorbidities were present in 79.8% of the patients with NV and in 55.9% with V ($p < 0000$). The most frequent comorbidity was cardiovascular diseases in NV (38.2%) and neoplasia in V (23.7%). The mean Rockall score was 3.9 (±1.9) in NV and the mean Child-Pugh score was 7.5(±3.0) in V. At admission, mean Hb value was 9.2 gr/dl (±2.6) for NV and 8.9 gr/dl (±2.0) for V ($p < 0.006$) and hemodynamic instability was presented in 7.6% of NV and in 10.1% of V ($p < 0.000$). More than half of the patients were transfused (58.2% of NV and 67.9% of V; $p < 0.000$). The mortality rate was 5.6%. in NV vs 11.9% in V ($p < 0.000$). In both groups, mortality was due to the bleeding episode only in 24% of the patients, while in the rest was related to underlining diseases (e.g. multiorgan failure, respiratory and/or renal failure, table 1).

| | Variceal bleeders | Non Viriceal bleeders |
|---|---|---|
| **Death causes** (%) Related to the bleeding episode Not directly related to the bleeding episode | 24.1 75.9 | 24.4 75.6 |
| **Causes of death (%)** | | |
| Liver failure | 32.3 | – |
| Multiorgan failure | 24.6 | 26.3 |
| Terminal neoplasia | – | 21.8 |
| Respiratory failure | 12.3 | 16.3 |
| Sepsis | 10.8 | – |
| Myocardial infarction | | 8.2 |
| Hepatic encephalopathy | 6.1 | – |
| renal failure | 3.1 | 5.4 |
| Stroke/intestinal infarction | – | 1.8 |

**Conclusion:** Comorbities are common both in variceal and in non-variceal bleeders and negatively impact on the mortality of GI bleeders, accounting for about 75% of the causes of death in this population.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1235 FEASIBILITY OF FULL-SPECTRUM ENDOSCOPY GASTROSCOPY, PREVALENCE OF DUODENAL PERIAMPULLARY DIVERTICULA, AND FUTURE OF DIRECT PER-ORAL CHOLANGIOSCOPY

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**Introduction:** The recently developed Full-Spectrum Endoscopy (FUSE) gastroscopy platform, which has two lenses, one at the front and one on the side of the distal tip, has a much wider field of view (245°) than a standard forward-viewing single-lens gastroscope (150°), which facilitates the detection of hidden lesions, such as duodenal periampullary diverticula (PAD) or ampullary lesions. Duodenal PAD is difficult to find with traditional gastroscopy, despite the 11–40% detection rate with endoscopic retrograde cholangiopancreatography (ERCP). However, no study has examined the prevalence of duodenal PAD in the general population using conventional gastroscopy rather than ERCP.
**Aims & Methods:** We were the first to use the FUSE system in Korea and this is the first report of a feasibility study on the use of this new system and on the prevalence of duodenal PAD in a Korean population using FUSE gastroscopy. We suggest that direct per-oral cholangioscopy can be performed with a modified FUSE gastroscope without radiation exposure. We explored the efficacy and safety of FUSE gastroscopy in a retrospective, single-center feasibility study performed between February 1 and December 31, 2015. After excluding 210 cases, 611 subjects (310 males, age 17–81 years) underwent FUSE gastroscopy for screening, surveillance, diagnostic evaluation, or a therapeutic procedure. We also assessed the prevalence and association of duodenal PAD.
**Results:** All of the diagnostic and therapeutic interventions, including endoscopic submucosal dissection (ESD), were performed successfully using the FUSE gastroscope. The insertion and guidance of endoscopic accessories to desired locations were convenient, and no gastroscopy was aborted because of equipment malfunction or failure. The duodenal periampullary portion was detected in all patients by FUSE gastroscopy without adverse events or complications. The prevalence of duodenal PAD was 20.5% (n = 125) and there were 2 (1.6%), 14 (11.2%), and 109 (87.2%) cases of types I, II, and III duodenal PAD, respectively. Gender and age were not associated with duodenal PAD, although subjects with non-specific gastric symptoms (epigastric pain, bloating, or indigestion) and colonic diverticula were more frequent in the duodenal PAD group ($p < 0.05$, Table). If another working channel were made on the side-lens portion then direct per-oral cholangioscopy would be possible with the aid of a baby scope, without radiation exposure.
Basic Charateristics and Prevalence of Duodenal Periampullary Diverticula (PAD)

| | All subjects | Subjects with Duodenal PAD | Subjects without Duodenal PAD |
|---|---|---|---|
| Number (%) | 611 | 125 (20.5%) | 486 (79.5%) |
| M:F | 310:301 | 67:58 | 243:243 |
| Age, mean ± SD | 47.5 ± 12.9 | 48.2 ± 13.3 | 47.4 ± 12.8 |
| ≤ 40, n (%) | 174(28.5%) | 33(26.4%) | 141(29%) |
| 41–60, n (%) | 341(55.8%) | 67(53.6%) | 274(56.4%) |
| ≥ 61, n (%) | 96(15.7%) | 25(20%) | 71(14.6%) |
| With gastric symptoms, n (%) | 337 (55.2%) | 79 (63.2%) | 258 (53.1%) |
| With colonic diverticula, in additional colonoscopy cases, n (%) | 73/364 (20.1%) | 23/73 (31.5%) | 53/291 (18.2%) |

**Conclusion:** This first Korean trial found that FUSE gastroscopy is feasible, safe, and effective. Moreover, using FUSE gastroscopy, the prevalence of duodenal PAD in the general population could be analyzed without using ERCP. In the future, FUSE gastroscopy is expected to be useful in direct per-oral cholangioscopy without radiation exposure.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1236 ENDOSCOPIC PUNCTURE-SUTURE DEVICE IN CLOSING THE DEFECT OF THE GASTRIC WALL AFTER FULL-THICKNESS RESECTION: SURVIVAL PORCINE STUDY

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**Introduction:** Closure of gastric wall defects after endoscopic full-thickness resection remains a clinical challenge. We aimed to introduce an endoscopic puncture-suture device (EPSD) for the closure of such defects. To evaluate the safety and efficacy of the EPSD in gastric wall defect closure by comparing outcomes after the metallic clips closure method after endoscopic full-thickness resection.
**Aims & Methods:** Twenty-four mini pigs (weight range 20–25 kg) were randomly divided into two groups. The EPSD was used in the experimental group and metallic clips were used in the control group. Twelve pigs were randomly assigned to each group. Six pigs underwent endoscopic full-thickness resection (EFTR) on the anterior wall of the gastric body, while the other six pigs underwent the same procedure on the posterior wall. The diameter of the resection margin was 2 cm. The EPSD and metallic clips were applied to close the defects. Pre- and postoperative routine blood testing, serum ions, C-reactive protein, duration of the resection and closure, incidence of operative complications, and wound recovery were compared and analyzed according to the closure approach.
**Results:** For defects in the same sites, compared with the metallic clips method, EPSD significantly reduced closure time (27.5 minutes vs. 8 minutes in the anterior wall and 26.8 minutes vs. 7.8 minutes in the posterior wall). Both groups had comparable chemical examination index. The incidence of pneumoperitoneum in anterior-wall full-thickness resection was 83.3% (10/12). In the posterior wall full-thickness resection group, this incidence was 8.3% (1/12). Wound recovery in all subjects was satisfactory.
**Conclusion:** The EPSD is a device which can quickly, easily, safely, and effectively close the gastric wall defect after EFTR.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1237 PRELIMINARY REPORT OF A NEW SCISSOR-LIKE DEVICE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR SAFE AND EFFECTIVE TREATMENT OF ZENKER'S DIVERTICULUM

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**Introduction:** Endoscopic therapy of Zenker's diverticulum is based on cutting the septum between the diverticulum and the esophageal lumen by using lasers, staplers, harmonic scalpels, argon plasma coagulation, or needle knives. Most recently, a new scissor-like device with serrated jaws for endoscopic submucosal dissection (ESD) was introduced. The device is fully rotatable and available in different lengths. In addition, the outer edges are insulated to minimize the risk of damaging tissue.
**Aims & Methods:** First study to prospectively assess the potential of the new scissor-like ESD device for treatment of Zenker's diverticulum. Therefore, patients with Zenker's diverticulum were prospectively enrolled. With the patient under conscious sedation a conventional feeding tube was first placed through the nose of the patient. A single channel endoscope with a clear distal cap was used for all examinations. The scissor like device allows for selective grasping and cutting of the septum and the muscle fibers. Performance characteristics, complications and follow-up data were recorded.
**Results:** Five patients were treated yet (mean age 74 years, Range 65–80 years; 3 female). Mean diameter of Zenker's diverticulum was 32 mm (Range 20–50 mm). Mean procedure time was 4.8 minutes (Range 3–7 minutes). No bleeding was recorded. In one case opening of the deep muscle layer occurred which was closed with 3 hemoclips. Postprocedural course was uneventful in all cases. All patients described significant symptom improvement without any relapsing symptoms (mean follow up time 10 months).
**Conclusion:** Endoscopic treatment of Zenker's diverticulum with the new scissor-like ESD device is fast and efficient. These preliminary findings should now be evaluated in future prospective, controlled multicenter Trials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1238 THE USE OF A NOVEL EXTRACELLULAR SCAFFOLD MATRIX FOR HAEMOSTASIS DURING ENDOSCOPIC RESECTION IN PATIENTS AT HIGH RISK OF BLEEDING: A LITTLE GOES A LONG WAY

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**Introduction:** Endoscopic resection (ER) is an effective method for treating early gastrointestinal (GI) neoplasia. ER although safe, carries the risk of bleeding (particularly with deeper dissection) which can be as high as 15%. Conventional methods of controlling bleeding include the use of diathermy and clips. A novel extracellular scaffold matrix (Purastat®) has recently been approved for haemostasis within the GI tract. This self-assembling peptide forms a transparent gel that can be applied over the bleeding area.
**Aims & Methods:** We aimed to evaluate the technical feasibility of delivering this agent at the bleeding site as well as its safety and efficacy as a haemostatic agent. A secondary objective was to ascertain the mean volume of Purastat® required to cover the entire resection base when used as prophylaxis in this high-risk population. This was a prospective observational study of patients undergoing complex ER in a tertiary referral centre from December 2015-March 2016 where Purastat® was used. Purastat® was used prophylactically to prevent bleeding after resection of high risk lesions or for primary haemostasis when active bleeding was encountered during the procedure. Data was collected on patient demographics, lesion characteristics, technical feasibility of Purastat® application, haemostasis and complications. Surface area of the resection base was calculated using the equation: Area = $2*\pi*R*L*\%$circumferential extent/100. R=radius and L=length of lesion.
**Results:** Purastat® was used in 30 patients during the study period. The average age of the patients in this study was 72.3 years with a male:female ratio of 2:1. 25 patients (83.3%) had endoscopic submucosal dissection whilst 5 (16.7%) had endoscopic mucosal resection. 18 (60%) of the lesions were in the oesophagus, 5 (16.7%) each in the stomach and colon and 2 (7.4%) in the duodenum. 3 patients were fully anticoagulated on warfarin which was withheld pre- procedure. 6 patients were on single antiplatelet therapy (not withheld). Mean lesion size was 3.47 cm.
**Conclusion:** Purastat® is a safe device which is easy to use with an effective application system allowing quick and guaranteed delivery during endoscopic resection. Purastat® can limit the use of diathermy needed for intraprocedural bleeding control and reduces the risk of delayed bleeding. Unlike clips, Purastat does not pose a technical challenge to continuing endoscopic resection in view of its transparent nature. In addition, only a small amount of this agent is needed to effectively cover the resection base for prophylaxis in lesions with a high risk of bleeding. Further prospective randomised controlled trials are needed to understand the exact role of this novel haemostatic agent.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1239 ENDOSCOPIC TREATMENT FOR METACHRONOUS EARLY GASTRIC CARCINOMA IN A RECONSTRUCTED GASTRIC TUBE AFTER RADICAL OPEREATION FOR ESOPAGEAL CARCINOMA

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**Background:** The incidence of metachronous early gastric carcinoma in a reconstructed gastric tube after radical operation for esophageal carcinoma has increased as a result of the significant advances in both diagnostic procedures and anti-cancer therapy. We investigated the characteristics of the gastric tube cancer with endoscopic therapy and outcome after treatment.
**Patients and Methods:** We assessed 14 patients and 22 cases of metachronous gastric tube cancer reconstructed with a gastric tube after esophagectomy for esophageal cancer at the Department of Surgery, Keio University School of Medicine, from 2009 to 2015. We investigated the timing of tumor origin, therapeutic approach, disease complication, tumor size, invasion depth, histopathology and long-term outcomes.
**Results:** 13 patients were male and 1 patient was female. The median age at which gastric tube cancer was detected was 71.6 years (range 49–81 years).The median time from esophagectomy to detection of gastric tube cancer was 7.9 years. All patients were treated using endoscopic submucosal dissection (ESD). The median size of tumor was 22.7 mm (range 10–70 mm), depth of tumor invasion was M in 15 cases, SM1 in 2 cases, SM2 in 2 cases, and more than SM2 in 1 case. Curative resections were performed in 5 cases (23%) and non-curative resections were in 17 cases (77%). 4 cases were detected recurrences; local recurrence in 3 cases and peritoneal dissemination in 1 case. The post-operative complication observed only in one case with a delayed perforation of a reconstructed gastric tube after ESD. As emergency operation, the resection of gastric tube with transthoracic approach and the thoracic tube drainage was performed. Currently, 13 cases remain alive and only one case has died by recurrence.
**Conclusion:** As recent advances in diagnostic and treatment modalities for esophageal cancer improve patient survival after radical esophagectomy, the occurrence of a gastric tube cancer continues to increase. Surgical removal of the reconstructed gastric tube has been reported to be a more invasive procedure with high risk of postoperative morbidity and mortality. An extended indication of endoscopic resection should be considered for which are possible to non-curative cases. However endoscopic resection is widely used for the treatment, we experienced one case with a serious complication of delayed gastric perforation which was never reported before. Further investigations are required to establishment a treatment strategy for lesions that does not fulfill the indication for endoscopic resection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1238 Table 1:** Purastat® Use for Prophylaxis and Primary Haemostasis

| Purastat® Use | Mean Lesion Size (cm) | Haemostasis achieved with Purastat® only | Haemostasis achieved with Purastat® + heat/clips | Delayed Bleeding (1 month) |
|---|---|---|---|---|
| Prophylaxis alone (n = 13) | 3.95 | N/A | N/A | 0 |
| Primary Haemostasis (n = 10) | 3.10 | 8 (80%) | 2 (20%) | 0 |
| Primary haemostasis + prophylaxis (n = 7) | 3.10 | 5 (71.4%) | 2 (28.6%) | 0 |

Purastat® on its own was effective in stopping bleeding in 13/17 cases (76.5%). Purastat® was easy to deliver with no incidences of catheter blockage and apposed well to the ER base during application. The mean surface area of the resection base for the entire cohort was 12.97cm$^2$ requiring a mean Purastat® volume of 2.81mls, equating to 0.22mls/cm$^2$. On follow up in 1 month, there were no postprocedural complications or delayed bleeding in any of the 30 patients.

## P1240 ENDOSCOPIC RESECTION FOR HYPERPLASTIC GASTRIC POLYPS: IS IT JUSTIFIED?

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**Introduction:** A small proportion (1.5%–3% of the cases) of hyperplastic polyps shows dysplasia or intramucosal carcinoma. Thus, it is usually recommended to resect supracentimetric polyps for histologic examination. Recently, we experienced an extensive hyperplastic recurrence following ESD for a large hyperplastic polyp with dysplasia and then we decided to evaluate the results of endoscopic resections for those hyperplastic polyps in order to measure effectiveness and morbidity.

**Aims & Methods:** We conducted a retrospective analysis of all endoscopic resections for hyperplastic polyps over 1 cm performed in two tertiary care centers between 2012 and 2016. Histologic examination and follow up endoscopies were recorded in order to evaluate effectiveness and morbidity of those resections.

**Results:** 59 hyperplastic polyps were resected in 35 patients (23 male, 12 female). Among the 35 patients, 2 were cirrhotic patients and 11 had *H. Pylori* infection. 21 polyps were resected by endoscopic submucosal dissection (ESD), 35 with endoscopic mucosal resection (EMR), 3 were resected by hybrid technique (ESD and EMR). Histologic examination showed 4 dysplastic lesions (7.2%) including 1 adenocarcinoma in situ, 1 high-grade dysplasia and low-grade dysplasia in 2 cases. The mean size of the lesions was 26 mm (6–59 mm). 26 patients had a single polyp although 9 patients had at least 2. Regarding the complications, there was no perforation. Only one patient experienced a severe bleeding (1.8%) two days after EMR with hemorrhagic shock. He had multiple hyperplastic polyps on a watermelon stomach. One of them had been resected by ESD with no adverse event during a first endoscopy procedure and then 8 were resected in a second procedure (4 by EMR technique and 4 by ESD technique) complicated by a hemorrhagic shock. 56 polyps were resected ''in sano'' (healthy margins resection). In the follow up, 5 recurrences appeared after initial resection by EMR in 3 cases, hybrid technique in one case, and ESD in one case. Resection was considered R0 and complete in 4 of the 5 recurrences. Two of them had an infection with *Helicobacter Pylori*. There was no other factor that may explain the recurrence for the other 3 patients (no cirrhosis, no Hp). The first patient was referred for the resection of 3 hyperplastic polyps. He underwent 4 new resections (3 by EMR technique and 1 by hybrid technique), there were hyperplastic polyps every time, never dysplasia and he is followed up every year. The second one underwent a new resection by ESD technique and had no reccurence. The third one underwent 2 new resections (1 by EMR technique and 1 by hybrid technique) and had no recurrence currently. The fourth one underwent a new resection by hybrid technique, and had no recurrence currently. The fifth one underwent a new resection by ESD, and had no recurrence currently.

**Conclusion:** Hyperplastic polyps are benign lesions with rare dysplastic evolution. In our study with 55 lesions, only 7.2% were dysplastic and only 1 adenocarcinoma was found (1.8%). ESD and EMR were relatively safe with only one adverse event with severe bleeding. The main issue of such resections is the local recurrence rate of 7.2% even if the initial resection was curative and R0. Optimal management of these lesions is not yet established but endoscopic resections seem to be a good and safe option but needing a early follow up to detect and resect local recurrences before large extensive relapse.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1241 ACCREDITATION OF ENDOSCOPY SERVICES IN ITALY:PRELIMINARY RESULTS

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**Introduction:** High-quality endoscopy delivers better health outcomes and a better patient experience (1), but there are clinically important differences in quality of endoscopy and patient outcomes between services across Italy.

**Aims & Methods:** Aim of this work is to describe the accreditation project of endoscopy services in Italy. In 2014 the Italian Society for Digestive Endoscopy (SIED) decided to develop a project for professionally lead service accreditation in collaboration with an independent organization with a special focus on health sector. In the same year SIED created a Quality Assessment Team made up of five endoscopists with a special interest on quality assurance and one representative of the certification company to provide a platform for definition of service and professional standards and leverage to achieve them. The Quality Team, in collaboration with the representatives of the Italian Nurse Association (ANOTE), prepared national endoscopic standards, taken from international professional organizations and guidelines and these standards were published on the SIED's website. Leadership and organization of the service, information and communication, quality and safety of the endoscopy (esophagogastroduodenoscopy, colonoscopy, retrograde colangiopancreatography and percutaneous endoscopic gastrostomy), integration of care, training of trainees and of health professionals entering the service and reprocessing, were included in the accreditation scheme. Performance measures have been applied in the pre, intra and post-endoscopy time periods with a particular interest for process measures and outcome measures rather than structural measures that reflect aspects of healthcare infrastructure harder to change. These performance measures were approved by the SIED's National Committee. Because quality improvement requires political will, we always research, at a local level, support from hospital management. Before the site-visit the endoscopy services used a standard framework as a template for quality improvement. The standard framework took the form of a checklist, which ensured that services did not miss out key aspects of care, enabled them to prioritise work, to evaluate levels of achievement within each domain (such as patient information, safety or reprocessing), to allow tracking of progress and, eventually, to assess readiness of the site-visit for accreditation. Peer review assessors were not reimbursed for the time, but only for travelling and lodging expenses.

**Results:** So far, the peer review components of the accreditation process (two endoscopists, a representative of the accreditation body and a nurse) have locally assessed, against clearly defined criteria, 13 endoscopy services scattered all over the Italian Regions. Seven endoscopy services, that fulffilled the prepared standards, have been accreditated, three have not satisfied the SIED accreditation criteria, and will receive another site-visit in three-six months, two services are under evaluation. One centre has not been accreditated because performance criteria had not been met. Accreditated services will provide informations on a regular basis, between peer visits, to satisfy the accrediting body that standards are being mantained, and to avoid that hospitals may comply with accreditation criteria only during the site-visit period as a ''one-off focused activity'', with doubtful impact on the ability of accreditation to bring about continuous improvements.

**Conclusion:** At the beginning of our program we have observed that external inspection of compliance with standards may improve healthcare organisation and professional behaviour. Considering the time, effort, and resources needed for accreditation programmes, it is essential to collect other data to prove the effectiveness of such programmes and on future improvements.

**Disclosure of Interest:** M. Capelli: Maurizio Capelli works for Kiwacermet certification of products and services
All other authors have declared no conflicts of interest.

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## P1242 HIGHEST POWER MAGNIFICATION WITH NARROW-BAND IMAGING IS VERY USEFUL TO DIAGNOSE THE MARGINS OF EARLY GASTRIC CANCERS, ESPECIALLY AFTER HELICOBACTER PYLORI ERADICATION

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**Introduction:** It has been reported that a characteristic of gastric cancer which was discovered after eradication of *Helicobacter pylori* (HP) is that diagnosis of the margins of these cancers by magnifying endoscopy is difficult due to the presence of non-neoplastic epithelium (1), but observation conditions such as magnification, etc. were not constant, so in order to examine the diagnosis capability of magnifying endoscopy must be performed under constant observation conditions.

**Aims & Methods:** Aims: To examine diagnostic accuracy for delineation of gastric cancer margins, post HP eradication gastric cancer and HP non-eradication gastric cancer, at different magnification ratios using magnifying endoscopy with narrow-band imagine (NBI). Methods: Out of 125 early gastric cancer lesions removed by ESD consecutively at our hospital from August 2013 to December 2015, 2 lesions were exempted because presence or absence of HP infection was unclear, along with 2 non-differentiated adenocarcinoma lesions, leaving a target 121 lesions which were divided into Group A (post HP eradication gastric cancer group, 42 lesions) and Group B (HP non-eradication gastric cancer group, 79 lesions). For each group the accurate diagnostic rate of delineation by magnifying endoscope was then determined retrospectively at the respective magnifications. Low power magnification was defined as a focal length of approximately 4 mm, using the VS (vessel plus surface) classification system for magnifying endoscope diagnostic criteria of Yao et al (2). Endoscopic examination was conducted in the order of normal endoscopy, NBI low power optical magnification observation, and NBI highest power optical magnification observation, with marking conducted 3–5 mm outside the demarcation line (DL) of lesions. Successful lesion was defined as cases where endoscopically the DL all around the lesion was consistently identifiable and pathologically consistent.

**Results:** Patient background (Group A vs Group B) was average age: 71.4 vs 74.1, tumor diameter (mm): 17.3 vs 18.2, tissue type (tub1/tub2): 32/10 vs 72/7. The accurate diagnosis rate was 95.2% (40/42) for Group A, and 98.7% (78/79) for Group B, with no significant difference seen. In misdiagnosed cases, histologically there was a moderately differentiated adenocarcinoma and a fundic gland mucosa type gastric cancer in Group A, and a moderately differentiated adenocarcinoma in Group B. When evaluated at the respective magnification ratio, successful rate at low power magnification was 59.5% (25/42) for Group A, and 83.5% (66/79) for Group B, with successful rate significantly lower for Group A ($p = 0.0038$). When evaluated histologically, in Group A many cases involved non-cancerous epithelium, and in observation limited to the surface microstructure under low power magnification, diagnosis of the margins of gastric cancer post HP eradication were considered difficult.
**Conclusion:** Highest power magnification with NBI is very useful, and by performing highest power magnification observation it is possible to perform range diagnosis at the same standard as for HP non-eradication gastric cancers. Whereas under low power magnification, there are many post HP eradication gastric cancer lesions for which range diagnosis is difficult.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1243 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 & Methods:** The aims of this study were to compare endoscopic subtumoraldissection (ESD) with surgical resection for the removal of GSET-PM. Patients/Methods: 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 5 cm 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 group.
**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 of Interest:** All authors have declared no conflicts of interest.

### P1244 A COMPARISON OF EFFICACY, OUTCOME AND COMPLICATIONS OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH THE OLYMPUS SECOND GENERATION ELECTROSURGICAL KNIFE DUALKNIFEJ™ VS OLYMPUS FIRST GENERATION DUALKNIFE™. A SINGLE CENTRE RETROSPECTIVE STUDY


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**Introduction:** Recent improvements in the Olympus second generation electrosurgical knife (Olympus DualKnifeJ™ KD-655) used in endoscopic submucosal dissection (ESD) has the improved features of allowing concurrent injection for mucosal raise in between submucosal dissections. The DualKnifeJ has become available since October 2015. Currently, more evidence is required in determining whether the second-generation knife is indeed superior and safe when compared to its first-generation counterpart.[1,2] Our centre has used the Olympus first generation electrosurgical knife (Olympus DualKnife™ KD 650) till end of December 2015 and had since then changed to using the second generation knife. This study aims to provide further comparative evidence between the two knives.
**Aims & Methods:** A single-centre, retrospective analysis was conducted by analysing the ESD database of our hospital. All patients included in the study had ESD done for either oesophageal, gastric or colonic lesions in between the periods of June 2013 till March 2016. Data compared included average procedure time, midazolam usage, intraoperative complication and en-bloc resection rates.
**Results:** In the first generation DualKnife™ group (A group), there were 266 cases (M:145, F121, age range 35–95, oesophageal ESD 14%, gastric ESD 41%, colonic ESD 45%). In the DualKnifeJ™ group (B group), there were a total of 36 cases (M:16, F20, age range 35–98, oesophageal ESD 3%, gastric ESD 47%, colonic ESD 50%). The average procedure time was 56 minutes in the A group and 59 minutes in the B group, with average midazolam dosage of 3.79 mg and 3.7 mg respectively. The en-bloc resection rates were 94% in the A group (mean lesion size 33.11 mm) and 100% in the B group (mean lesion size 34.1 mm). Intraoperative complications included hypotension (A:65%, B:77%), desaturation (A:40%, B:44%), bradycardia (A:14%, B19%), tachycardia (A:11%, B8%) and Mallory Weiss tear (A:1%, B:5%). Although minor bleeding had occured intraoperatively during dissection in all cases in both groups, there were no related fatal events, all were successfully treated and there was no perforation in both groups. Overall, there was no statistical difference in terms of recorded complications between the 2 groups ($p = 0.49$).
**Conclusion:** Our data provides evidence that the new DualKnifeJ is comparatively as safe as the first-generation dual knife, has better en-bloc resection rate, indifferent in intraoperative complication rate and the cost difference is minimal. From an operator's perspective, with DualKnifeJ, the dual function of submucosal injection during dissection allows much better submucosal visualisation, reduces time and potential scope position loss whilst awaiting change to the injection needle. We conclude that the DualKnifeJ is preferred in comparison with the first-generation dual knife.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1245 PREDICTORS FOR FOREIGN BODY PRESENCE AT ENDOSCOPY IN FOREIGN BODY INGESTION - A PROSPECTIVE STUDY


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**Introduction:** Foreign body ingestion (FBI) and food impaction (FI) are one of the most frequent emergencies in gastroenterology. It is important to know the proportion of patients in which a foreign body is present in the upper digestive tract, since it is frequently reported that a large proportion of ingested foreign bodies pass throughout the upper digestive tract without clinical consequences. Identification of risk factors for foreign body / food impaction presence is also important in order to define the need for urgent endoscopy and also its timing.
**Aims & Methods:** The aim of this study was to identify predictors of foreign body presence in the upper digestive tract and to assess its management and complications. Methods: This was a prospective unicentric cohort study including consecutive patients with FBI or suspected FI during one year. Continuous variables were compared with independent samples t-test while chi-square test was used for categorical variables; relative risks were computed where adequate.
**Results:** 262 patients were included (171 with FBI, 91 with suspected FI). FI patients were more frequently female and were significantly older when compared with patients with suspected food impaction ($p < 0.05$). Dysphagia was significantly more frequent in the FI group, while odynophagia and foreign body perception were the predominant symptoms in FBI. In the FBI group, the foreign body was identified in the upper digestive tract in 43.2%; older age and earlier presentation to the emergency department were significantly associated with foreign body presence in multivariate analysis. Compared with fish bones, meat bones were more frequently found (49% vs 41%), although the difference was not statistically significant. Foreign body extraction was not possible in 4.8% due to technical difficulties and were referred for rigid esophagoscopy. In FI, there was a known esophageal disease (mainly stricture) in 34.4%. Food impaction was confirmed in 81.1% and was successfully solved in 95.8%. Roth net was the most used instrument in FI, while foreign body forceps was preferred in FBI. The need to use a second instrument was more frequent in FI (23.2% vs 11.3%, $p = 0.06$). Overall, anesthesia was required in 6.5% and major complications occurred in 0.4% (1 perforation).
**Conclusion:** Almost half of the patients with FBI have a foreign body found at esophagogastroduodenoscopy; older age and early presentation to the emergency department increase the likelihood of foreign body presence. FB removal and food impaction resolution were achieved in >95%.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1246 AVAILABILITY OF LAPAROSCOPIC AND ENDOSCOPIC COOPERATIVE SURGERY: AN INTERNATIONAL QUESTIONNAIRE SURVEY

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**Introduction:** Laparoscopic and endoscopic cooperative surgery (LECS) has been developed as a minimally invasive surgery for localised gastrointestinal neoplasms, and it uses a combination of both laparoscopy and endoscopy. LECS is applied predominantly for gastric subepithelial tumours at present[1)] and the indication is expected to be further expanded to gastric cancer[2)] or other organs[3)]. However, there are several issues to be addressed in order to establish and disseminate this methodology worldwide.

**Aims & Methods:** We planned to conduct an international survey for availability of LECS by gathering current opinions regarding LECS from overseas experts in the field of gastrointestinal endoscopy and surgery.

In February 2016, a web-based survey was administered to 35 overseas endoscopists who had given or organized international live demonstrations or had conducted endoscopic training courses. The questionnaire included 22 questions, which were mainly multiple choice questions and were related to the feasibility, efficacy and acceptability of this procedure, e.g. the respondent's opinion on and experience in performing LECS as well as other relevant issues. The responses were collected within 1 month and assessed thereafter.

**Results:** A total of 25 experts (71%) responded to this survey. A main affiliation of the respondents was gastroenterology and hepatology (76%), endoscopy and endoscopic surgery (16%) or surgery (8%). The concept of LECS was known among 96% of respondents. LECS was considered to be easily accessible (12%), accessible (52%), doable (28%) and to be quite beneficial (84%) or partially beneficial (8%), whereas only 40% of respondents had direct experience in performing LECS. Although the respondents considered that the introduction of LECS would be welcome (84%) or acceptable (16%), they expected an acceptable procedure time to be no more than 1 hour (16%) and 2 hours (64%). Furthermore, they considered the minimum estimated fee to be USD 3,000 (20%), 4,000 (24%) or over 5,000 (8%).

**Conclusion:** LECS was considered feasible, beneficial, and acceptable but currently has limited availability. In the permeation of this procedure, the issue of cost-effectiveness remains to be addressed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1247 LONG-TERM OUTCOMES AFTER NON-CURATIVE ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER ACCORDING TO THE ADDITIONAL TREATMENT

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**Introduction:** A few patients with non-curative resection of endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) do not undergo additional gastrectomy due to old age, comorbidities or poor general condition. However, there are concerns about safety and long-term outcomes of patients with non-curative resection.

**Aims & Methods:** Of 1,525 patients who underwent gastric ESD for EGC, 291(19.1%) patients with non-curative ESD from 2007 and 2014 were reviewed retrospectively. Non-curative resection is defined as histologically positivity of the resected margins, lymphovascular infiltration, piecemeal resection or beyond expanded criteria for ESD. Recurrence was defined as local and residual recurrence of EGC after non-curative resection.

**Results:** A total 291 patients with more than 6 months follow-up periods were analyzed and the mean (± S.D.) follow up duration was 43.4 (± 22.9) months. Of them, 160 patients (55.0%) and 37 patients (12.8%) underwent surgery and endoscopic treatment after non-curative resection, whereas 94 patients (32.3%) were observed. 75 (25.8%) patients had lymphovascular infiltration, 150 (51.5%) patients had EGCs that had margin positive resection, 36 (12.4%) patients had EGCs that had not en bloc resection. The disease-free survival (DFS) rates was higher in patients with endoscopic treatment than with observation group (86.5% and 81.9%, $p < 0.001$). When we compared three subgroups, the 5-year overall survival (OS) was statistically significant in patient with additional surgery group, additional endoscopic treatment group, and observation group (97.5%, 94.6% and 90.8%, respectively, $p = 0.031$). Among additional endoscopic treatment group, 4 patients (10.8%) developed recurrence of EGC. Interval for additional endoscopic treatment after 3 months was an independent predictor of recurrence in multivariate analysis (HR 30.000, 95% CI, 1.834 – 490.786, $p = 0.017$).

**Conclusion:** In this study showed that compared to observation group, additional surgery or endoscopic treatment improved overall survival and disease-free survival in patients with non-curative ESD. Also, early additional endoscopic treatment within 3 months, was favorable to DFS and OS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1248 DO VISIBLE VESSELS WITHIN THE POST-ENDOSCOPIC MUCOSAL RESECTION (EMR) DEFECT PREDICT POST-EMR BLEEDING?

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**Introduction:** Clinically significant post EMR bleeding (CSPEB) is the most frequent serious complication after wide-field endoscopic mucosal resection (EMR) of laterally spreading lesions ≥ 20 mm (LSLs). Visible vessels within the post EMR defect (PED) present themselves as logical targets for prophylactic treatment to prevent CSPEB. However the clinical significance of these vessels is largely unknown. In the majority of studies risk factors identified for CSPEB include right colon location, lesion size and aspirin use.

**Aims & Methods:** We aimed to evaluate the clinical significance of the various endoscopic features of the post EMR defect including visible vessels. A prospective study of LSLs ≥ 20 mm referred for EMR at a single tertiary referral center was performed. Data collection included patient and lesion characteristics, defect features including submucosal vessels, submucosal haemorrhage, fibrosis, fat and exposed muscle, and the rate of CSPEB. CSPEB was defined as any bleeding occurring after the completion of the procedure necessitating emergency department presentation, hospitalization or reintervention. CSPEB was compared to features of the PED to detect significant associations, using $chi^2$ or Fisher's exact tests. Significant univariate variables were taken forward for binomial logistic regression modelling.

**Results:** Over 60 months, to April 2016, 576 lesions (51.5% located proximal to the transverse colon) in 576 patients (mean age 66.8 years, 50.7% male) were eligible for analysis. The frequency of CSPEB was 35/576 (6.1%). Defect features and statistical analysis are outlined in table 1.

No features of the PED, including number of visible vessels (median 3, IQR 0.25–7.75, $p = .308$), diameter of largest vessel (14/165 >0.5 mm (8.5%), $p = .853$) and herniation of vessels (12/146 (8.2%), $p = .620$), were significantly associated with CSBEP at univariate analysis and were therefore not used in the multivariate model. However, vessels were more often seen in the left colon (76% vs 63.9%, $p = .002$), and these were significantly larger (19.6% vs 9.2% ≥ 1 mm, $p = .008$), more numerous (median 4 (IQR 2–6) vs 3 (IQR 1.25–4.1) vessels, $p < .001$) and showed more often herniation (32.6% vs 21.7%, $p = .005$).

**Table 1:** Defect and procedural features in patients with clinically significant post EMR bleeding (CSPEB) as compared with patients with no CSPEB.

| | Lesions (N = 576) | Univariate P | Multivariate P |
|---|---|---|---|
| **Defect features** | | | |
| Presence of visible vessels (%) | 402 (69.8) | .314 | / |
| Presence of arteries | 34 (5.9) | .713 | |
| Presence of veins | 394 (68.4) | .141 | |
| Number of visible vessels (median, IQR) | 3 (0.25–7.75) | .187 | / |
| Herniation of vessels (%) | 12/146 (32.6) | .620 | / |
| Estimated diameter of largest vessel (in comparison to snare wire) (%) ° ≤1 mm ° >1 mm | 21 (60.0) 6 (17.1) | .446 | / |
| Intraprocedural bleeding (%) | 182 (31.6) | .429 | / |
| Submucosal haemorrhage | 58 (10.1) | .787 | / |
| **Procedural features** | | | |
| Aspirin use within 7 days (%) | 53 (9.2) | .009 | .005 |
| Lesion size ≥ 40 mm (%) | 26 (4.5) | .001 | .002 |
| Lesion location in the right colon (%) | 23 (7.8) | .051 | .017 |

On multivariate analysis CSPEB was associated with use of aspirin within 7 days (RR 3.31, 95% CI 1.5–7.6, $p = .01$), size ≥ 40 mm (RR 3.54, 95% CI 1.6–7.8, $p = .001$) and right colon location (RR 2.508, 95% CI 1.177–5.344, $p = .017$).

**Conclusion:** Number, size or presence of herniation of vessels within the PED does not predict CSPEB. Vessel number, size and herniation is significantly greater in the left colon however the bleeding rate is less. Other features within the PED also do not predict CSPEB, including submucosal haemorrhage and intraprocedural bleeding.

The visible vessels within the PED should not be considered a therapeutic target for prevention of CSPEB and should not be used for risk stratification of CSPEB. Lesion location and size are the dominant risk factors for CSPEB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1249 RANDOMIZED COMPARATIVE EVALUATION OF AN ESD SELF-LEARNING SOFTWARE IN FRANCE AND JAPAN


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**Introduction:** Endoscopic submucosal dissection is currently the reference method to achieve an en bloc resection for large lesions of the digestive tract. Nevertheless, it is a difficult and risky technique with a long learning curve. To reduce the morbidity related to the first procedures, it is recommended to attend training courses with animal models. Self-training programs could have a role in parallel to simplify access to training and at least to learn the initial skills. Self-learning software to assist students in the first steps of ESD has been recently developed. We designed this study to evaluate the impact of such a tool on the ESD learning curve for French and Japanese students using a bovine colon model.
**Aims & Methods:** A prospective randomized comparative study enrolled 39 students (31 in France and 8 in Japan) experienced in interventional endoscopy but not in ESD. Each student was randomized in one of the two groups and performed 30 ESD on a 30 mm large simulated rectal lesion in a retroflexed endoscopic view. The software group used the self-learning software whereas the control group only observed an ESD procedure movie. No other technical explanation was given to both groups. Procedure duration, resection completeness, perforation rate and the specimen size and surface were assessed.
**Results:** 39 students performed 1170 ESD (software group: 19 students, 570 ESD) (control group: 20 students, 600 ESD) with respectively 404 (71.0%) successes (resection of a specimen in less than 75 min) in the software group versus 367 (61.0%) in the control group ($p = 0.030$). Amongst the 1113 successes, the complete resection rate was 76.2% in the software group versus 67.4% in the control group ($p = 0.031$). Among the successes, the perforation rate and the procedure duration were not significantly different with 22 (3.8%) vs 29 (4.8%) ($p = 0.271$) and 34.1 (+/- 13.4) versus 32.3 (+/- 14.0) min ($p = 0.517$) respectively. Regarding only the 30$^{th}$ procedure of each student, the rate of complete resection was superior in software group with 84.2%versus 50.0% ($p = 0.005$). The rate of success in the French group was 77.3% versus 21.7% ($p = 0.001$) in the Japanese group. This significant difference was not explained by the lower experience of Japanese students but probably linked to the learning design (5 consecutive days versus non consecutive Saturdays). For the animal model training, a minimum number of 20 procedures seems required.
**Conclusion:** The use of this ESD self-learning software is effective to improve the quality of resection compared to a standard teaching method with procedure movies for trainees experienced in endoscopy but not in ESD. This result suggests to incorporate such self-learning software in the ESD teaching program.
**Disclosure of Interest:** T. Ponchon: Olympus grants
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All other authors have declared no conflicts of interest.

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### P1250 COMPUTER-BASED AUTOMATIC DIFFERENTIATION OF NEOPLASTIC AND NON-NEOPLASTIC POLYPS WITH THE APPLICATION OF DEEP STRUCTURED LEARNING ALGORITHMS OF A CONVOLUTIONAL NEURAL NETWORK – PRELIMINARY RESULTS


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**Introduction:** Deep learning algorithms and convolutional neural network (CNN) is recently applied in many areas related to medical imaging. Automated computer assisted differentiation between neoplastic and non-neoplastic colorectal polyps based on digital chromoendoscopy pictures could support resect and discharge strategy after polypectomy of minute polypoid lesions detected during colonoscopy.
**Aims & Methods:** The aim of our present preliminary study was to evaluate the usefulness of deep structured learning algorithms for automated computer-based differentiation of hyperplastic and adenomatous colorectal polyps. Patients referred for screening colonoscopy were prospectively enrolled and 100 polyps of 75 patients were detected. All colonoscopies were accomplished with HD zoom colonoscope of Fujinon EC-590ZW/L series. Based on our previous results FICE-filter 4 with 50 times digital magnification [red, green, and blue (RGB) wavelengths of 520, 500, and 405 nm, respectively] provided the best images for evaluating the vascular and surface (pit) pattern for colorectal adenomas. Therefore, optical zoom and HD surface pictures of the colorectal polyps were digitally stored with FICE-filter 4 and with 50 times magnification. Histopathology of the lesions was classified after pathological evaluation from endoscopic resection, polypectomy or biopsy specimens. Regions of interests (ROI) sized of 275x275 pixels were manually selected on captured digital pictures of the surface of the colorectal polyps, and then uploaded to the ERSATZ labs cloud-based deep learning platform.
**Results:** According to the histopathological results, 59 adenomas (5 with severe dysplasia), and 41 hyperplastic polyps were captured, classified and selected for further computer analysis. From the 100 images, 60 images are selected as a training set, and the remaining 40 images are selected as a validation set. Training images were fed to the cloud-based CNN with automatic parametric variables and cropped into pixels with the proposed deep structured learning algorithm. During validation, 91.60% of the test pictures are classified correctly as neoplastic or non-neoplastic polyp region.
**Conclusion:** Computer-assisted differentiation of colorectal polyps is a promising tool to assist differentiation of hyperplastic and adenomatous polyps detected with digital zoom chromoendoscopy. Further improvement of accuracy of the deep learning algorithms may be achieved by increasing the total number of polyps uploaded to the training set and also tuning the parametric variables of the CNN.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1251 COLD SNARE POLYPECTOMY DOES NOT INCREASE THE POSSIBILITY OF RESIDUAL POLYP: A PROSPECTIVE SINGLE-ARM OBSERVATIONAL TRIAL


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**Introduction:** Generally, cold snare polypectomy (CSP) is considered a safe procedure for subcentimetric polyps, although incomplete assessment of the horizontal margin (HM) can often occur [1].
**Aims & Methods:** This study aimed to investigate the residual polyp rate after CSP for resecting subcentimetric neoplastic polyps. This was a prospective, single-arm observational study conducted at a referral cancer center in Osaka, Japan, between March and December 2013. The protocol of these prospective trials was registered in the University Hospital Medical Network Clinical Trials Registry (UMIN-CTR, UMIN 000010879). Patients aged 20 years or older with adenomas smaller than 10 mm (1–9 mm) in diameter were enrolled in this study. CSP was performed until no polyp was visible. Each polyp base was then resected

using additional endoscopic mucosal resection (EMR), leaving a clear margin of 1–3 mm of surrounding non-neoplastic mucosa. The removed polyps and marginal specimens were retrieved with suction through a working channel of the colonoscope and trapped in a bottle attached to the suction route.Each trapped specimen (polyp and marginal specimen) was stored in separate jar containing formalin 20% without pinning on a plate. The fixed specimen were sectioned serially at 2-mm intervals and subjected to histological examination. Any neoplastic tissue observed in the marginal specimen was considered residual polyp. The primary endpoint was residual polyp rate after CSP, compared with historical data of conventional EMR.

**Results:** Of the total 138 patients screened, 126 patients, with 362 subcentimetric polyps diagnosed as neoplastic lesions, were enrolled. The additional EMR could not be performed on 10 (2.8%) of the 362 lesions because of technical difficulties. Two marginal specimen could not be retrieved, and one marginal specimen was contaminated with a removed polyp. Additionally, two additional EMR were recognized as protocol violation, resulting exclusion from the analysis. Therefore, we assessed 347 subcentimetric polyps. The median age of the patients was 71 (IQR 64–75) years. Patients were 83 (65.9%) men and 43 (34.1%) women. Their morphologies were 279 (77.1%) protruded/sessile (0–Is) lesions and 83 (22.9%) superficial/elevated (0–IIa) lesions. The median (IQR) size of the detected polyps was 5 (3–6) mm. Of these polyps, 269 (74.3%) were diminutive (1–5 mm) and 93 (25.7%) were small (6–9 mm). Among 347 evaluable marginal specimens, histopathological diagnosis indicated that 332 (95.7%) were non-neoplastic lesions and 15 (4.3%) were neoplastic polyps. Thus, we considered the unadjusted incidence (90% confidence interval [CI]) of residual polyp after CSP was 4.3 (2.5–6.1)%. No differences were observed in polyp size, age, location, morphology, or operator experience between lesions with and without residual polyp. In the removed polyps, polyp involvement at the lateral margin could not be assessed correctly (HM X) in 229 (68.8%) polyps.

**Conclusion:** The incidence of residual polyp after CSP was 4.3% and did not increase compared with conventional EMR in the previous report.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1252 INTERNAL HEMORRHOIDS ARE A COMMON CAUSE OF SEVERE HEMATOCHEZIA BUT PATIENTS HAVE MUCH BETTER OUTCOMES THAN THOSE WITH OTHER COLON DIAGNOSES

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**Introduction:** Internal hemorrhoids are the most common cause of colonic bleeding in ambulatory outpatients [(1)]. However, the prevalence and clinical outcomes of patients hospitalized with severe hematochezia from bleeding internal hemorrhoids have not been reported.

**Aims & Methods:** Our aim was to compare demographics and outcomes of patients hospitalized with severe hematochezia from internal hemorrhoids compared with other colonic diagnoses. For methods, consecutive patients with severe hematochezia admitted between 1995 and 2015 to our two tertiary referral academic medical centers, seen by the GI consultation services, and having urgent colonoscopy after colon purge, were prospectively evaluated. Clinical, laboratory, endoscopic and outcome results (rebleeding, surgery, time to discharge and death) up to 30 days or hospital discharge were retrospectively analyzed. SAS was used for data management and analysis. Bivariate analyses were carried out, using Chi-square and $p < 0.05$ was considered statistically significant.

**Results:** A total of 709 patients with colonic or hemorrhoidal causes of severe hematochezia were included, 76 patients with internal hemorrhoids (10.7%) and 633 patients with other colonic diagnoses (89.3%). Internal hemorrhoids were the third most common cause of colonic hematochezia after colonic diverticular disease (32.4%) and ischemic colitis (12.1%). For the hemorrhoid group, bleeding started as outpatient in 62 patients (81.6%) and as inpatient after admission for unrelated co-morbidity in 14 patients (18.4%). In the 76 patients with internal hemorrhoids compared to patients with other colonic diagnoses, gender, ethnicity, number of red blood transfused for resuscitation or hemoglobin were not significantly different. In the hemorrhoids group, there was significantly lower mean age ($62.3 \pm 15.5$ vs $66.6 \pm 15.5$, $p = 0.02$), Aspirin use (25.0% vs 40.7%, $p = 0.0079$), shock or hypotension (13.2% vs 24.3%, $p = 0.030$), cardiac failure (59.2% vs 79.0%, $p = 0.0006$) and metabolic history (42.1% vs 59.2%, $p = 0.018$). Prevalences of alcohol and liver disease were significantly higher in the hemorrhoid group (respectively 29.0% vs 10.7% $p < 0.0001$ and 40.8% vs 20.7%, $p = 0.0002$). Emergency endoscopic treatment rates were significantly lower in the hemorrhoid group (23.7% vs 38.1%, $p = 0.0449$) and consisted of banding (77.8%) or Bicap (22.2%). For clinical outcomes, see table 1. Internal hemorrhoid patients had significantly better results than patients with other colon diagnoses. Table 1: Clinical outcomes after endoscopic diagnoses of patients with internal hemorrhoids compared to patients with other colonic diagnoses.

**Conclusion:** 1) Internal hemorrhoidal bleeding was the third most common cause of severe hematochezia in hospitalized patients. 2) Compared to other colonic causes of severe hematochezia, patients with internal hemorrhoidal bleeding were younger; fewer used aspirin before bleeding, had cardiac failure, hypotension or metabolic disorders, but more drank alcohol or had liver disease. 3) Outcomes were better for the hemorrhoid group with reduced time to discharge and lower rates of rebleeding or urgent endoscopic treatment.

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### P1253 WHAT IS THE CULPRIT LESION FOR INTERVAL CANCER AFTER COMPLETE COLONOSCOPY?

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**Introduction:** Interval cancer (IC) has become a focus of attention as likely representing ''missed'' or ''rapidly growing'' lesions in colonoscopic screening for colorectal cancer (CRC), and it is currently assumed in Western countries that sessile serrated adenoma/polyps (SSA/P) may be the likely culprit lesion for IC in many cases.

**Aims & Methods:** To determine the culprit lesion for IC. This study included a total of 6163 patients (females/males, 2334/3829) undergoing complete colonoscopy (CC) procedures performed by the same single endoscopist (TF) at TFCL during the period between 2003 and 2015. IC was defined as all T1/T2 tumors detected during CC within 3 years following the CC procedures with removal of all neoplastic lesions.

**Results:** In the 6163 patients, CC detected 76 traditional serrated adenoma (TSA), 373 SSA/P, and 9025 adenomas, with the cancer stage being Tis in 411 lesions, T1 in 45, and $\geq$ T2 in 93. Of these, 8 were determined as cases of IC and were detected during CC examinations performed at a mean interval of 19 months (9–29 months), with the gross appearance of IC in these cases being all flat and depressed (IIa + IIc, 3; LST-NG with pseudo-depression, 4; and IIc, 1). Again, of the 8 cases of IC, 1 was located in the cecum, 1 in the ascending colon, 3 in the transverse colon, 1 in the descending colon, and 2 in the rectum, with the mean tumor diameter being 22.6 mm (13–35 mm) and the depth of invasion being T1 (slight invasion) in 3, T1 (massive invasion) in 3 and T2 in 2, therapeutic endoscopic procedures required in 5 (EMR, 2; P-EMR, 2; and ESD, 1), surgical resections required in 4, and lymph node metastasis found in 1. In this last case, the lesion was shown to be a IIa + IIc T2 lesion measuring 18 mm and present in the recto-sigmoid curve and. In this patient, a total of 5 polyps were removed in the CC performed 1 and 2 years ago, while a mean total of 3 polyps were found prior to detection of IC, with 3 lesions found to be T0.

**Conclusion:** Flat-depressed lesions may represent the likely culprit lesion for interval cancer, given their morphological features that make them difficult to detect by colonoscopy. As detection of these lesions is thought likely to be affected by such factors as blind spots in colonoscopy and bowel preparation and the lesions may be characterized as rapidly growing, colonoscopic examinations for CRC need to be performed with these lesions in mind.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**P1252**

| Diagnoses (N) | Urgent hemostasis* | Lesion bleeding* | Surgery* | Mean no. of hospital days** | Mean no. of days in ICU** | Mean units of RBC's after diagnoses** | death* |
|---|---|---|---|---|---|---|---|
| Internal hemorrhoids (76) | 18 (23.7) | 5(7.1) | 1 (1.3) | $3.7 \pm 5.1$ | $0.78 \pm 3.5$ | $0.12 \pm 0.8$ | 2 (2.6) |
| Other colon Lesions (633) | 241 (38.1) | 104 (16.4) | 47 (7.4) | $8.01 \pm 9.6$ | $3.49 \pm 8.0$ | $0.90 \pm 3.2$ | 35 (5.6) |
| p value | 0.045 | 0.024 | 0.044 | $<0.001$ | $<0.001$ | 0.03 | 0.28 |

ICU = Intensive care unit; RBC = red blood cell, * Number (%) ** Values shown are mean ± standard deviation

## P1254 IS IT EFFECTIVE TO ADD A REMINDER PROPOSING VIRTUAL COLONOSCOPY OR COLON CAPSULE EXAMINATION TO IMPROVE PARTICIPATION TO COLORECTAL CANCER SCREENING IN PATIENTS WITH POSITIVE FECAL OCCULT BLOOD TEST WHO REFUSED COLONOSCOPY?

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**Introduction:** Colorectal cancer screening strategy is based in France on the search for occult bleeding in the stool. However, 13% of patients with a positive test never undergo further colonoscopy. These patients are then recontacted by the management structure but if they don't answer at the end of the complete process of recovery, they are not further invited to the screening program. This study conducted with the screening associations of Rhône « Ademas- 69» and Loire « Vivre » aimed to compare randomly the invitation to perform colonic capsule or virtual colonoscopy in those patients in order to propose them a less invasive strategy.
**Aims & Methods:** Patients identified by the two associations of screening who had a complete recovery procedure without any answer were targeted and receive solicitation offering a re-examination or by colonic capsule or Virtual Colonoscopy after randomization. The objectives of the study were to assess the rate of response, their participation in the proposed additional examination and the results in terms of detection and consequences on the future management of the patient.
**Results:** 756 patients (388 females, 368 males) were targeted with 378 proposals of colonic capsule and 378, Virtual Colonoscopy. Among them, 139 responses were obtained: 70 patients (9.2%) accepted to come for a new examination (38 in the colonic capsule group, 32 in the colonoscopy virtual group), 69 patients/families (9%) called to explain their refusal (26 had already had a colonoscopy, 22 refused categorically any new procedure, 17 wanted to consult their doctor for more information and 4 had died). After 70 patients having made an appointment, only 47 patients (31 females, 66%) finally realized examination with respectively 19 colonic capsules (14 females) and 28 virtual colonoscopies (18 females). 5 patients finally chose an optical colonoscopy instead of the examination proposed. 17 patients (28%) did not come to the scheduled examination including 14 in the colonic capsule arm. Among the 19 colonic capsules performed, 6 adenomas or cancers were detected, as well as 6 hyperplastic polyps and 4 other bleeding lesions. Among the 28 virtual colonoscopies, 5 adenoma or cancer and 3 hyperplastic polyps were detected as well as 4 other potentially bloody lesions. Taking into account these results, 15/19 colonic capsules versus 10/28 virtual colonoscopies have resulted in an additional indication of colonoscopy, 1/19 capsule an indication of proctoscopy against 1/28 virtual colonoscopies and 2/19 against 11/28 gave rise to a new screening two years later by FOBT. Actually, only 6 of the 29 patients (20.7%) with colonoscopy indications finally accepted to perform the procedure.
**Conclusion:** An additional reminder offering a less invasive (colonic capsule or colonoscopy virtual) examination for patients with FOBT + without previous colonoscopy is not effective since only 9.2% of patients responded positively. Among them, only 66% finally underwent the proposed examination or the colonoscopy originally proposed. Contributions to the colonic capsule and Virtual Colonoscopy were not different. The number of lesions detected by the colonic capsule (n = 12/19) was slightly more important than in Virtual Colonoscopy (n = 12/28) as several comparative studies have previously shown. In addition, the colonic capsule leads to propose optical colonoscopy or proctoscopy in 57.4% of the patients examined, which seems to support the importance of optical colonoscopy in first intention in these patients detected by FOBT +.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1255 ENDOSCOPIC TREATMENT OF GASTROINTESTINAL TRACT PERFORATIONS, ANASTOMOTIC LEAKAGES AND FISTULAS USING THE OVER-THE-SCOPE-CLIP SYSTEM (OVESCO): TWO-CENTRE EXPERIENCE

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**Introduction:** Anastomotic leakages, fistulas and iatrogenic perforations of gastrointestinal tract remain the mayor problems in gastrointestinal surgery and endoscopy. An over-the-scope clip (OTSC) OVESCO has been developed for the closure of small mural defects and bleeding ulcers (1). The OTSC produces more durable closure than standard endoclips because of its ability to grasp more tissue, include the entire thickness of the visceral wall, and apply a greater compressive force (2).
**Aims & Methods:** A retrospective analysis of prospectively collected data in cases of restitution of the digestive tract integrity with OTSC System in two Lithuanian hospitals was performed. Data including technical aspects, clinical outcomes and closure rates were recorded.
**Results:** 20 patients from two Lithuanian hospitals (Vilnius University Hospital Santariskiu Klinikos and National Cancer Institute) were treated applying OTSC clip. Overall 24 procedures were made, and 27 clips were applied between 2013 and 2016. Indications: anastomotic leak and fistula – 13 cases (9 cases - esophageal fistula); iatrogenic lesion of the colon – 4 cases; perforation due to necrotic pancreatitis after multiple operations – stomach and duodenum – 2 cases; leak of the esophageal suture after perforation with the foreign body – 1 case. Mean age of the patients (8 female, 12 male) was 65 years (range 35–85 years). Mean size of the fistula/leak was 1.2 cm (range 0.2–4.0 cm). We achieved complete defect closure at initial procedure in 15/20 of the cases (75%). The completeness of the closure has been checked radiologically and/or by injecting methylene blue solution immediately after the clip application. In 3 cases two clips were applied during initial procedure. In 4 cases clip application was repeated when clinically and radiologically signs of fistula recurrens appiered. In cases of big (> 2.0 cm) lesion closure clinical outcome revealed worse compared to small (< 1.2 cm) defects. At the remote period in 13/20 patients (65%) fistulas remained closed. We argue that unsuccessful clinical outcome is affected not only by technical details, but also by severe general patient condition (for example caused by sepsis or poor nutritional status). Iatrogenic perforation of the colon was closed successfully in all cases.
**Conclusion:** 1. OTSC® System could replace or supplement in certain cases traditional surgical approach in the treatment of fistula, perforation or anastomotic leak. 2. At the remote period in 65% cases fistula remained closed. 3. OTSC® should be available in the endoscopy units where interventional procedures are carried on.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1256 COST-EFFECTIVENESS ANALYSIS OF COLONOSCOPY COLORECTAL CANCER SCREENING AMONG CYSTIC FIBROSIS PATIENTS

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**Introduction:** Survival for Cystic Fibrosis (CF) patients has greatly increased over the past 30 years. However, with increasing survival, CF patients also become at risk for other diseases. Recent studies, for example, showed that CF patients have a 7-fold higher risk of colorectal cancer (CRC) compared to the general population. Screening has the potential to reduce the burden of CRC in CF patients. The aim of this study is to estimate costs and benefits of CRC screening in CF patients and determine the optimal screening strategy from a cost-effectiveness perspective.
**Aims & Methods:** The Microsimulation Screening Analysis (MISCAN)-Colon micro-simulation model was adjusted to reflect CRC risk and life-expectancy in CF patients and subsequently used to simulate a cohort of 10 million 30-year old CF patients in 2017. Costs and benefits of 50 colonoscopy screening strategies with various age to start (30,35,40,45,50) and end screening (55,60,65,70,75) as well as screening intervals (5 and 10 years) were evaluated. We performed incremental cost-effectiveness with a willingness to pay threshold of 100,000$ per life-year gained to determine the optimal CRC screening strategy.
**Results:** Without screening, the model predicted 8 per 1,000 CF patients to die of CRC. Colonoscopy screening every 10 years from age 45 to 65 was predicted to prevent more than 60% of these deaths. The optimal screening strategy was colonoscopy every 5 years between ages 40 and 75 with an incremental cost-effectiveness ratio of 92.547$ per life-year gained. The amount of CRC cases and death prevented with this strategy were 8.74 and 5.70 per 1.000 CF patients, respectively and representing an incidence reduction of 41% and a mortality reduction of 72% relative to no screening.
**Conclusion:** This study suggests that CRC screening in CF patents is cost-effective, and because of their higher risk, the CF patients could be screened from an early starting age with a shorter screening interval.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1257 MODIFIABLE FACTORS ASSOCIATED WITH PATIENT-REPORTED PAIN DURING AND AFTER SCREENING COLONOSCOPY

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**Introduction:** Pain associated with colonoscopy is a major barrier to participation in colorectal cancer screening.
**Aims & Methods:** The aim of this analysis was to identify modifiable factors associated with patient-reported pain during and after colonoscopy performed in programmatic screening setting. We performed a cross-sectional analysis of database records from a population-based colonoscopy screening program (PCSP) in Poland. Since 2014 a validated tool for assessment of patients' experience with colonoscopy (the Norwegian Gastronet project) is being routinely used in centers enrolled in the PCSP. The Gastronet is a questionnaire assessing patient-reported pain during and after colonoscopy, rated on a 4-point scale (no, little, moderate and severe pain). The Gastronet is to be filled in by all screenees on the day after colonoscopy. For the purpose of this analysis we included a derivation cohort of screening colonoscopies performed in 2014 in 17 centers by 44 endoscopists and validation cohort of screening colonoscopies performed in 2015 in 23 centers by 85 endoscopists. All endoscopists included contributed at least 100 procedures. We used ordered multivariable logistic regression models adjusted for age to estimate odds ratios (OR) and 95%CI for one point increase in pain scores associated with patient body mass index (BMI), previous abdominal surgery, endoscopists experience, specialty, cecum intubation rate (CIR) and adenoma detection rate (ADR), endoscope generation, type of screening facility, bowel preparation and use and type of sedation.
**Results:** Of 8760 screening colonoscopies included in 2014 and 26,626 in 2015, 5412 (62.6%) and 17,176 (65.2%) valid Gastronet questionnaires were returned. Overall 2573 (47.28%) in 2014 and 8595 (49.83%) patients in 2015 reported no pain during colonoscopy. A significant variation based on use and type of sedation was observed (for 2014 cohort, 38.38% of patients in case of no sedation, 46.58% of patients in case of sedation without anesthesiologist and 85.98% of patients in case of sedation with anesthesiologist). Results for 2015 cohort were similar. Several patient, procedure, endoscopist and center factors were independently associated with lower odds of painful colonoscopies. On the other hand, surgical specialty of endoscopist and public type of endoscopy center were associated with higher odds of painful colonoscopies (Table 1). As for pain after colonoscopy, an association of lower odds for pain with male sex, sedation and endoscope generation was observed. Contrary, higher odds were observed for surgical specialty of endoscopist and public type of center (Table 1). Previous abdominal surgery, preparation method, endoscopist adenoma detection rate (ADR) and endoscopist experience were not associated with pain during and after colonoscopy. The kappa value for the agreement between endoscopist- and patient-reported pain was 0.23 and 0.22 for 2014 and 2015 cohort respectively. Moreover, endoscopists tended to report better procedure tolerance than reported by patient.
**Conclusion:** Several independent, modifiable factors associated with pain during and after colonoscopy were identified. There was poor agreement between endoscopist- and patient-reported pain scores.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1258 A REVIEW OF CURRENT PRACTICE IN FLEXIBLE SIGMOIDOSCOPY - CAN WE DO BETTER?

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**Introduction:** In March 2013, the British Society of Gastroenterology produced a position statement on indications for flexible sigmoidoscopy. We wished to assess whether or not referral practice in our large teaching hospital trust was adhering to this guidance.
**Aims & Methods:** We undertook a retrospective audit to examine referral practice for flexible sigmoidoscopy. We identified all flexible sigmoidoscopies performed between 2nd January 2015 and 1st April 2015 from our endoscopy reporting system. From 816 identified cases, we excluded 136 cases which included Bowelscope, ileal pouch anal anastomosis and rectal stump surveillance as well as erroneous duplicate entries. The remaining 680 cases were then assessed as being appropriate or not according to the BSG criteria.
**Results:** The average age of the study population was 53.7 with an age range of 16–95. There were 321 males and 359 females. Of 680 symptomatic cases referred for flexible sigmoidoscopy, we found that 229 (33.7%) were not appropriate. The test was incomplete in 212 cases (31.2%). The most common reason for an incomplete test was inadequate bowel preparation in 87/212 cases (41%). 498/680 flexible sigmoidoscopies were abnormal. 18 cases resulted in a diagnosis of colorectal cancer with 6 de novo diagnoses. Of the 229 patients in whom flexible sigmoidoscopy was deemed to be an unsuitable first line investigation, 66 went on to have further radiological or endoscopic investigation, but 155 had no further investiagtion, of whom 86 were dicharged with no further follow up after the index sigmoidoscopy. The average time interval between the index sigmoidoscopy and a further appropriate test was 73.7 days with a range of 3 to 268 days.
**Conclusion:** Unfortunately, in this study, approximately one-third of flexible sigmoidoscopy requests were not consistent with current best practice guidelines. Furthermore, completion rates are poor and time intervals to more appropriate investigation appear too long. Better case selection has the potential to lead to more appropriate utilisation of endoscopic resources. In this study, this translated to an additional capacity for 460 colonoscopies or equivalent endosopic investigations per annum.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1259 PREDICTED ADENOMA DETECTION RATE (ADR) AND COMPARISON TO ACTUAL PHYSICIANS' ADR

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**Introduction:** The proportion of patients in whom at least one adenoma is detected during colonoscopy, i.e. adenoma detection rate (ADR), is inversely associated with the development of interval colorectal cancer (CRC). Current guidelines recommend an ADR of ≥25% (≥30% for male, and ≥20% for female patients). However, the strict definition (screening, average risk) and

**P1257 Table 1:** – Multivariable odds ratios for one point increase in pain level during and after colonoscopy. Includes data from derivation cohort (2014) and validation cohort (2015). * OR and 95% CI adjusted for age and sex. $ N/S – not significant. & BBPS – Boston Bowel Preparation Scale. #1st: Olympus CF-Q140 and 145, Pentax EC3830, 3870.3885; 2nd: Olympus CF-Q165 and 170, Pentax EC380FK2, Fujinon EC-530; 3rd: Olympus CF-Q180, H180, Pentax EX 3890Fi2, Fujinon EC-590; 4th: Olympus CF- H185, H190 and HQ190.

| Variable | Pain during colonoscopy | | Pain after colonoscopy | |
|---|---|---|---|---|
| | OR (95% CI)* 2014 | OR (95% CI)* 2015 | OR (95% CI)* 2014 | OR (95% CI)* 2015 |
| Patient factors | | | | |
| Sex (Male) | 0.39 (0.35–0.44) | 0.41 (0.38–0.44) | 0.83 (0.74–0.92) | 0.80 (0.76–0.86) |
| BMI (25–30 compared to <25) | 0.74 (0.65–0.85) | 0.77 (0.72–0.83) | N/S $ | N/S |
| BMI (30–50 compared to <25) | 0.59 (0.51–0.68) | 0.64 (0.59–0.69) | N/S | N/S |
| Procedure factors | | | | |
| Sedation without anesthesiologist | 0.51 (0.44–0.59) | 0.66 (0.61–0.72) | 0.78 (0.68–0.90) | 0.87 (0.80–0.94) |
| Sedation with anesthesiologist | 0.05 (0.04–0.07) | 0.01 (0.00–0.01) | 0.54 (0.45–0.65) | 0.37 (0.33–0.41) |
| Bowel preparation (BBPS& ≥2/2/2) | 0.73 (0.61–0.86) | 0.75 (0.68–0.83) | N/S | N/S |
| Endoscopist factors | | | | |
| CIR (≥95%) | 1.00 (0.99–1.00) | 0.71 (0.64–0.79) | N/S | N/S |
| Specialty (surgery) | 1.83 (1.60–2.08) | 1.22 (1.13–1.32) | 1.14 (1.00–1.29) | 1.16 (1.07–1.25) |
| Center factors | | | | |
| Type (public) | 1.41 (1.17–1.70) | 1.22 (1.11–1.33) | 1.24 (1.04–1.49) | 1.14 (1.04–1.24) |
| 3rd generation of endoscopes # | 0.49 (0.39–0.60) | 0.79 (0.70–0.89) | 0.71 (0.58–0.88) | 0.71 (0.63–0.80) |
| 4th generation of endoscopes # | 0.37 (0.29–0.48) | 0.57 (0.50–0.64) | 0.61 (0.48–0.77) | 0.59 (0.52–0.67) |

variation in physician panels, especially gender, makes it challenging to compare individual ADRs. We therefore aimed to develop a prediction model for adenoma detection and subsequently ADR.
**Aims & Methods:** Colonoscopy and demographic/risk factor data was used from the cross-sectional multicenter randomized EQUIP-3 study (NCT02325635) in which the GIQuIC national database was used. Patients ≥50 years undergoing screening or surveillance colonoscopy with adequate bowel preparation were included. Colonoscopy for genetic family cancer syndromes and surveillance of inflammatory bowel disease were exclusion criteria in the present study. The dataset was split into two cohorts based on performing center for geographical validation. We developed a prediction model for adenoma detection per patient using multivariable logistic regression. Missing data was handled by multiple imputation (20 multiple imputed datasets). The final model was selected by stepwise backward selection based on Akaike's information criterion and internally validated in the derivation cohort using bootstrap resampling (500 data sets). Goodness-of-fit was evaluated with calibration plots. The model was used to compare predicted and observed physicians' and centers' ADR. We present the development and internal validation of the model, with future geographical validation to be performed.
**Results:** A total of 10152 patients (male: n = 4839 [48%], median age: 60 [range: 50–90] years), undergoing colonoscopy in 5 centers by 35 physicians were included in the derivation cohort. The overall ADR was 36%, with a median of 35% (range: 19–53) per physician, and a median of 37% (range: 28–40) per center. The final model (table) showed only modest discriminative ability for adenoma detection (optimism-adjusted C-statistic: 0.62) based on five predictors. Interestingly, surveillance vs. screening, race, ethnicity and personal or family history of colorectal carcinoma were not selected in the model. The model slightly overestimated adenoma detection in patients with low and high observed prevalence of adenomas. The observed ADR per endoscopist and per center was lower than predicted for the lowest observed ADRs and higher than predicted for the highest observed ADRs.

**Table:** Prediction model for the detection of ≥1 adenoma.

| Predictor | Corrected[a]multivariableOR [95%-CI] |
|---|---|
| Age (per year increase | 1.02 [1.02–1.03] |
| Male sex | 1.72 [1.59–1.87] |
| BMI (per 1 kg/m$^2$ increase) | 1.02 [1.01–1.03] |
| ASA I ASA II ASA III or IV | ref 1.27 [1.15–1.40] 1.57 [1.33–1.86] |
| History of colorectal adenomas None Personal Family | ref 1.41 [1.29–1.55] 1.10 [0.88–1.37] |

OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiology physical status class [a]Corrected after internal validation using bootstrap resampling with shrinkage factor 0.97.

**Conclusion:** Patient risk factors, such as age, sex, ASA category and history of colorectal adenomas, could not completely predict adenoma detection and observed ADRs. Additional predictors which were not included in the database, e.g. smoking, alcohol and medication use, could possibly have added to the performance of the model. This data suggests that variation in raw ADR between physicians could likely be due to other factors, e.g. physician, procedural or technical factors, and not patient risk factors alone.
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All other authors have declared no conflicts of interest.

## P1260 FIRST CLINICAL EXPERIENCES OF A NOVEL ENDOSCOPIC OVER-THE-SCOPE CLIP SYSTEM

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**Introduction:** The over-the-scope clip (OTSC) system has showed promising results in the management of gastrointestinal (GI) fistulas, iatrogenic perforations, and bleedings. In addition, the OTSC-assisted endoscopic full thickness resection (EFTR) has been proposed as a therapeutic option for GI epithelial and submucosal tumors. Recently, a new OTSC device (Padlock Clip™, Aponos Medical, Kingston, NH, United States) has been introduced into clinical practice.
**Aims & Methods:** We retrospectively reported the results in the treatment of 14 patients in a 18-month period. The Padlock clip is a hexagonal nitinol ring with six inner prongs released by a delivery system that consists of an applicator cap, similar to the variceal band-ligation cap. The clip is preassembled in an opened position on the delivery system and it is released by a trigger cable parallel to the scope that is connected to a handle. After the suction of tissue within the cap to obtain adhesion to the instrument tip, the clip is released by the handle pushing wire within the cable. When deployed, the shape-memory effect and the high elasticity of nitinol cause the closure of the clip. Its six inner prongs penetrate and pull the tissue inward resulting in a pseudo-polyp of closed tissue. When performing EFTR, the tissue entrapped was resected with an oval snare above the closed clip applying cutting current.
**Results:** 8 out of 14 patients were treated for closure of GI fistulas (n = 4) or iatrogenic GI perforations (n = 2) and hemostasis of post-polipectomy bleeding (n = 2). Site of clipping was lower GI tract (rectum and sigma) in 5 cases and upper GI tract (stomach, duodenum) in the remaining cases. The clip was successfully delivered in 7 out of 8 cases and clinical success (closure of GI defect or bleeding resolution) was achieved in all cases. Endoscopic full thickness resection (EFTR) was performed to treat 6 patients with recurrent adenoma (n = 4), recurrent adenocarcinoma at ileorectal anastomosis (n = 1) and neuro-endocrine tumor of rectum (n = 1). Technical success was recorded in all cases. A complete intestinal wall resection and a R0 resection were achieved in 50% and 83.3% of cases, respectively. No complications were recorded. Endoscopic follow up ranged from 3 to 15 months and no recurrence was demonstrated either macroscopically or microscopically when the scars were biopsied.
**Conclusion:** This novel OTSC systems seems to be an effective and safe tool to treat GI deep wall lesions or GI bleeding and to perform EFTR. However, further studies are needed to confirm our preliminary results and to explore further indications in clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1261 SPLIT VS SAME-DAY REGIMES FOR BOWEL PREPARATION BEFORE COLONOSCOPY: A META-ANALYSIS OF PUBLISHED STUDIES

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**Introduction:** An adequate colon cleaning is essential for a good-quality colonoscopy and the split regimens (S) are actually considered the standard of care. However, 15–20% of patients still have an inadequate bowel cleansing after a split preparation. Recently a new regimen (same-day, SD) in which the purge is assumed the morning before the colonoscopy has been introduced, but published studies are underpowered and report controversial results.
**Aims & Methods:** Our aim was to assess the colon cleansing rate of split vs. same-day regimens. Published randomized clinical trials (1960–2015) comparing S vs. SD preparations in adults undergoing colonoscopy were selected using MEDLINE, the Cochrane Central Register of Controlled Trials, clinical trial.gov, ISI Web of Science. Search terms included bowel, preparation, colon, cleaning, colonoscopy, same-day and split. Rate difference (RD) of the degree of colon cleaning between split and same-day was the primary measure of treatment effect. Compliance (defined as the completion of at least > 75% of both doses of the purge) and presence of adverse events (nausea, vomiting, abdominal pain and abdominal discomfort) were secondary outcomes. **Statistics**: the meta-analyses were performed by computing RD using random-effects model, if heterogeneity was present. Egger's-Hardbord regression test was pre-defined statistical tests for publication bias assessment.
**Results:** From 122 initially screened abstracts, 11 full text studies were retrieved and a total of 12 treatment arms were analysed (1837 patients). Seven studies compared PEG vs. PEG, 1 sodium picosulfate vs sodium picosulfate, 1 sodium picosulfate vs. PEG and 3 PEG vs. sodium picosulfate. Overall, 88% (621/719) patients in the S group vs. 86% (570/688) in the SD group had an adequate bowel cleansing. Pooled RD was 2% [ (C.I.95% -1.6 to 5.6), heterogeneity chi-squared= 13.88 (d.f. = 8) p = 0.085; I-squared (variation in RD attributable to heterogeneity)= 42.4%, p = 0.280, Fig.1) ]. In all but one studies, split preparation was more effective than SD. Also, patients were more compliant and had slightly less adverse events with the split preparations but significant heterogeneity was present.
**Conclusion:** Data shows that split preparations give a similar adequate colon preparation compared with same-day preparations and with a better compliance and less adverse events.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1262 CLASSIFICATION OF CELL NUCLEI MORPHOLOGY OF EC FINDINGS IN COLORECTAL ENDOCYTOSCOPY

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**Introduction:** Endocytoscopy (EC) is a next-generation endoscopy that enables diagnostic imaging at 450× magnification. To date, excellent results have been achieved using EC classifications for qualitative diagnosis and assessment of depth of invasion of colorectal lesions (neoplasia/non-neoplasia accuracy: 96.5%; accuracy for carcinomas with massive submucosal invasion (SM-m): 96.3%).(1, 2)

**Aims & Methods:** 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 certain endoscopic factors in EC3a findings that could be indicators of SM-m. Among lesions that were observed by EC between May 2005 and January 2015, we retrospectively examined 277 lesions diagnosed as EC3a or EC3b, according to the EC classification. Patients with unclear glandular lumen were excluded. The presence or absence of four findings that are indicators of SM-m were examined by EC. The four factors were: (1) high degree of nuclear enlargement (HNE); (2) multilayered nuclei (MN); (3) marked dilation of vessels (MDV); and (4) fine granular structures (FGS). Based on the results, we thoroughly examined the diagnostic accuracy of EC3a findings in the diagnosis of depth of invasion.
**Results:** Based on the results of multiple logistic regression analysis, the factors useful for the diagnosis of SM-m were HNE ($p < 0.01$), MN ($p < 0.01$), and FGS ($p < 0.05$). Of these, HNE and MN had odds ratios $> 10$ and were considered important predictors of SM-m invasion. So we diagnosed the lesions which were positive for HNE and MN as EC3a-high grade, whereas lesions negative for such findings were diagnosed as EC3a-low grade. As a result, 32 of 119 lesions were diagnosed as EC3a-high grade. Of these, the final pathological diagnosis was SM-m in 19 lesions, and muscularis propria cancer (MP) in five lesions. The diagnostic efficiency was as follows: sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and positive likelihood ratio of 88.9%, 91.3%, 75.0%, 96.6%, 90.8%, and 10.2, respectively. In the EC diagnosis above, interobserver validation ($\kappa$) of the three endoscopists were 0.63, 0.64, and 0.69, whereas good values were obtained for intraobserver validation ($\kappa$) at 0.73, 0.79, and 0.67.
**Conclusion:** In the diagnosis of colorectal lesions by EC, EC3a findings of HNE and MN are important indicators of SM-m. Results also suggested that taking into consideration the findings as for EC3a may improve the diagnostic accuracy for SM-m.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1263 UNDERWATER EMR IS A SAFE AND A WELL-TOLERATED PROCEDURE: THE EXPERIENCE OF TWO UK CENTRES


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**Introduction:** Underwater Endoscopic Mucosal Resection (UEMR) is a relatively new technique, which has been developed for endoscopic resection of colonic lesions. In this technique, air or $CO_2$ insufflation is not required when performing EMR of lesions. We present here the experience of two UK centres.
**Aims & Methods:** The aim of this study was to assess the 1) feasibility of UEMR by endoscopists trained in traditional EMR, and 2) to assess the safety, tolerability, and effectiveness of UEMR. All of the procedures were performed by two experienced interventional endoscopists. Patient data was collected prospectively. A Hybrid technique, i.e. injection of lifting solution or use of Argon Plasma Coagulation (APC) together with UEMR, was employed if the lesion was traversing a fold/removed in retroflexed position or if there was remnant tissue post resection, respectively.
**Results:** From May 2015 to April 2016, a total of 41 patients (mean age 65.7 years, range 35–85, males n = 24) have had UEMR of 43 lesions performed by the two operators. The lesions (mean size 32.6 mm, range 7–160 mm) were located in right colon (n = 9), transverse colon (n = 2), left colon (n = 10), and rectum (n = 22). Seven of the lesions (16.3%) were recurrence post previous traditional EMR. The morphology of the lesions were either flat (n = 25) or sessile (n = 18). Hybrid technique was employed as following: Lifting (n = 20), APC (n = 4), and a combination of lifting and APC (n = 2). Histopathology of the lesions demonstrated low grade dysplasia (n = 34), high grade dysplasia (n = 6), and other (n = 3; One cancer and two serrated lesions). Complete endoscopic resection (at index procedure) was achieved in 42 out of the 43 lesions (97.7%); a large lesion (160 mm in size), which was crossing over two folds, was resected at two planned sessions. There were no perforations; however there were two cases of immediate bleeding (4.9%), which were controlled endoscopically during the procedure, and one case of delayed bleeding (2.4%), which was treated with Endoclot powder spray. The procedures, which were performed either with no sedation or analgesia (n = 12), with light sedation and analgesia (n = 22), or with Entonox inhalation as required (n = 7), were well-tolerated with a pain score of zero or one (zero = no pain; one = minimal pain).
**Conclusion:** In our experience, underwater endoscopic mucosal resection seems to be an effective, safe and a well-tolerated procedure, which can be performed by an endoscopist trained in traditional EMR. It can be an alternative to the traditional EMR, which requires either air or $CO_2$ insufflation. However, the insufflation of air or $CO_2$ significantly thins the colonic wall during the EMR, which may increase the risk of complications, but endoscopic ultrasound studies of the water-filled colon have shown that the colonic wall retains its natural thickness[1]. Follow-up data is required to assess the short- and long-term recurrence rate associated with UEMR.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1264 RANDOMIZED TANDEM COLONOSCOPY OF NARROW BAND IMAGING (NBI) AND WHITE LIGHT ENDOSCOPY IN PATIENTS WITH SERRATED LESIONS


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**Introduction:** Detection of serrated polyps is difficult due to their morphology and appearance. Sometimes, in patients with few serrated polyps, diagnostic criteria of Serrated Polyposis Syndrome (SPS) depends on identification of few additional polyps (e.g. 5 or more serrated polyps, 2 >= 10 mm). Patients with SPS are considered to be at increased risk of colorectal cancer and requires a close endoscopic follow-up. We hypothesize that NBI could improve the detection rate of serrated polyps compared with High Definition White Light Endoscopy (WLE) in patients not fulfilling completely the SPS.
**Aims & Methods:** We performed a randomized, cross-over trial at our institution from March 2015 to April 2016 of tandem colonoscopy using NBI and WLE in patients with at least 1 serrated polyp $\geq$10 mm, or in individuals with $\geq$3 serrated polyps independtly of the size, both proximal to the sigmoid colon. (ClinicalTrials.gov, NCT02406547). Patients were evaluated back-to-back by the same endoscopist, using both techniques randomly (1:1) NBI-WLE or WLE-NBI. All detected polyps were resected in each withdrawal. The main goal was to compare the rate of detected polyps between both techniques, the polyp miss rate and when it was possible, reassessing the diagnosis of SPS for an appropriate surveillance interval.
**Results:** A total of 41 patients were included. Mean age was 59.6 yrs (SD: 8.6); 53.7% males. The median time from last colonoscopy was 5 months (IQI: 3–7). Baseline characteristics were not different between NBI-WLE (n = 21) or WLE-NBI (n = 20). 246 suspected polyps were detected. Histology was obtained in 238, 28 (11.8%) with normal histology, 106 (44.5%) hyperplastic polyps, 28 (11.8%) sessile serrated polyps and 57 (23.5%) adenomas. No significant differences were observed in the median number of detected polyps by NBI (NBI-WLE group) and WLE (WLE-NBI group), 3 (IQI: 2–8) vs 2.5 (IQI: 1–4), respectively ($p = 0.15$). Moreover, there were no differences in the polyp miss rate of NBI and WLE, with 21.3% and 26.1% (OR 0.77, 95% CI: 0.43–1.39) respectively. An additional colonoscopy, independently of the technique identified 9 (22%) individuals that fulfilled the criteria for SPS.
**Conclusion:** NBI has a similar detection rate to WLE in patients with serrated lesions. A close follow-up to these patients could change the diagnostic to SPS about 1 in every 5 patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1265 SHOULD ALL SESSILE SERRATED ADENOMA/POLYPS BE TREATED?


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**Introduction:** Reports in Japan indicate that the type II-open pit pattern is a useful endoscopic finding for sessile serrated adenomas/polyps (SSA/Ps). The Japan Society for Cancer of the Colon and Rectum (JSCCR) has proposed the pathological diagnosis of SSA/Ps. Thus, although this criterion can be used to diagnose most typical SSA/Ps, consensus has not yet been reached on the treatment of the diagnosed lesions; the treatment is currently determined at the discretion of each institution. The absolute indication for resection (i.e., lesions that can be called high-risk lesions in advanced colorectal cancer) currently includes carcinoma in SSA/Ps and SSA/Ps with cytological dysplasia (advanced SSA/Ps); this clinicopathological characteristic is a very important index for establishing future SSA/P treatment.
**Aims & Methods:** The purpose of this study was to examine whether all SSA/Ps need to be resected. This study included 225 lesions in 183 SSA/P patients who

underwent endoscopic or surgical resection in our hospital between January 2008 and December 2015. There were 12 cases of carcinoma in SSA/Ps and 9 cases of SSA/Ps with cytological dysplasia. In addition to the conventional-pit pattern diagnosis, type II pit subclassification was used for magnifying endoscopic diagnosis. The pathological diagnosis of SSA/Ps was determined in accordance with the criteria proposed by the JCCCR. Patient characteristics (age and gender), conventional endoscopic findings (size, location, macroscopic type, color, and the presence or absence of mucus), and magnifying endoscopic findings were compared with the histopathological diagnosis. Molecular biological analysis was also performed for advanced SSA/Ps (A-SSA/Ps).

**Results:** Patient characteristics: The mean age was 64 years in the SSA/P group and 73 years in the A-SSA/P group. There were more men in the SSA/P group (56%; 116/204) and more women (76%; 16/21) in the A-SSA/P group. Conventional endoscopic findings: As found in earlier reports, in the A-SSA/P group, the lesions were more commonly on the right side of the colon, they were normal-colored or pale mucosa, and had abundant mucus; however, the lesion was macroscopically flat type with a higher elevation in 57% (12/21) of the patients of the A-SSA/P group. The lesion diameter was a median length of 10 mm in the SSA/P group and 20 mm in the A-SSA/P group. Magnifying endoscopic findings: Lesions exhibited several pit patterns in approximately 14% (30/204) of the SSA/Ps and all A-SSA/Ps. Particularly, 75% of carcinomas in SSA/Ps exhibited the type V pit pattern, with elevation and redness at the same site. Molecular biological analysis: Red, elevated lesions that were 15 mm in size in the ascending colon with a depression in the lesion center were analyzed. Most lesions exhibited type II-open pit and type IV pit patterns; however, type V pit pattern was observed in the depressed area. Upon diagnosis of SSA/P cancerization, endoscopic mucosal resection was performed. The pathological results were adenocarcinoma with SSA/Ps and depth was pTis. Analysis of sections containing cancer revealed BRAF mutation, MLH1 methylation, and microsatellite instability. These results appear to support the serrated pathway currently considered. Because we are also presently analyzing other cases of cancerization, we will report on this together with these results.

**Conclusion:** In the present study, the rate of concurrent SSA/Ps and cancer was 5.3%. Because resection was not necessarily performed of all SSA/Ps, we believe that the rate of concurrence is actually lower. Furthermore, carcinomas in SSA/Ps and SSA/Ps with cytological dysplasia present several surface microstructures compared to SSA/Ps and are highly likely to be elevated. Based on these results, if endoscopic diagnoses are carefully performed and A-SSA/Ps are effectively detected, not all SSA/Ps will require treatment. Further examination via a multicenter prospective study (with a larger subject sample, molecular biological analysis, and minimal bias) is anticipated.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1266 EFFICACY AND SAFETY OF THE NOVEL 1 L PEG AND ASCORBATE BOWEL PREPARATION NER1006 VERSUS SODIUM PICOSULFATE + MAGNESIUM CITRATE IN DAY BEFORE SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY DAYB


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**Introduction:** Successful colon cleansing enables effective colonoscopy. PEG based split dosing preparations are traditionally seen as the gold standard in cleansing, but many still require a high preparation volume intake. NER1006 is the first 1 L PEG3350 and ascorbate bowel preparation in phase 3 clinical development. The low volume of NER1006 is achieved through the use of ascorbate in the second dose only.

**Aims & Methods:** This phase 3, randomised, multicentre, colonoscopist-blinded, non-inferiority study assessed the efficacy, safety and tolerability of a day before split-dosing regimen of either NER1006 (NDB; evening time) or sodium picosulfate + magnesium citrate (SPM; regimen per label) in patients undergoing colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing success and 'Excellent plus Good' cleansing rate in the ascending colon including the caecum using the Harefield Cleansing Scale (HCS). Secondary endpoints included hierarchical evaluation of adenoma/polyp detection rates, and cleansing assessment using the Boston Bowel Preparation Scale (BBPS). Patient tolerability, acceptability and compliance were assessed using a questionnaire. Safety was monitored through adverse events reporting and clinical laboratory evaluation. The threshold for statistical significance in this study was $P < 0.025$.

**P1266 Table 1:** Patients, efficacy and safety

| Abstract legend | NER1006 day before split-dosing NDB | Comparator: sodium picosulfate/magnesium citrate SPM | CI for the difference [P value] NDB vs. SPM |
|---|---|---|---|
| **PATIENTS** | | | |
| Randomised patients [n] | 258 | 257 | |
| Mean age [years (SD)] | 54.6 (11.64) | 52.9 (13.35) | |
| Males / females [n] | 90 (34.9%) / 168 (65.1%) | 83 (32.3%) / 174 (67.7%) | |
| **EFFICACY** | **Primary analysis set, n = 250** | **Primary analysis set, n = 251** | |
| Primary endpoint: Patients with successful overall bowel cleansing efficacy (HCS) [n] | 155 (62.0%) | 135 (53.8%) | −0.50%* [0.038] |
| Supportive secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n] | 146 (58.4%) | 115 (45.8%) | n.a. |
| Primary endpoint: Excellent plus Good cleansing rate in colon ascendens [n] | 11 (4.4%) | 3 (1.2%) | −5.56%* [0.027] |
| Key secondary endpoint: Adenoma detection rate, colon ascendens | 6.4% | 4.0% | −6.35%; 11.12%** [0.154] |
| Key secondary endpoint: Adenoma detection rate, overall colon | 22.0% | 18.7% | −5.56%; 11.91%** [0.212] |
| Key secondary endpoint: Polyp detection rate, colon ascendens | 12.0% | 7.6% | −4.36%; 13.10%** [0.064] |
| Key secondary endpoint: Polyp detection rate, overall colon | 39.2% | 36.3% | −5.96%; 11.51%** [0.278] |
| Compliance rate (min 75% of both doses taken) [n] | 193 (77.2%) | 229 (91.2%) | n.a. |
| **SAFETY** | **Safety set, n = 235** | **Safety set, n = 241** | |
| All treatment-emergent adverse events [n] | 64 | 30 | n.a. |
| Patients with any related treatment-emergent adverse event [n] | 28 (11.9%) | 10 (4.1%) | n.a. |

* = 97.5% 1-sided CI; ** = 95% 2-sided CI; n.a. = not applicable

The confidence interval (CI) for the difference between the groups used a 10% margin to demonstrate non-inferiority vs. SPM.
**Results:** Patients were randomised to receive either NDB (n = 258) or SPM (n = 257). Demographic characteristics were similar between the two groups, as shown in Table 1. For both alternative primary endpoints, NDB was non-inferior (lower CI limit ≥ -10%) to SPM. NDB was also non-inferior to SPM in detecting adenomas and polyps, both in the ascending colon and in the overall colon (Table 1). Despite lower compliance rates for NDB vs. SPM, the overall bowel cleansing of NDB was non-inferior to SPM (Table 1). NDB had more treatment-emergent adverse events (TEAEs) than SPM, however the total numbers of patients with related TEAEs were low and no related event was serious. The most frequently reported related TEAEs were vomiting and nausea (NDB), and headache (SPM).
**Conclusion:** NER1006 as a day before regimen was non-inferior to SPM in achieving overall bowel cleansing success and an 'Excellent plus Good' cleansing rate in the ascending colon. NER1006 also showed non-inferior adenoma and polyp detection rates. Both treatments were well tolerated; most TEAEs were mild or moderate in severity and reflected the expected safety profile of respective treatments. The 1 L NER1006 administered the evening before colonoscopy offers comparable efficacy and safety to SPM.
**Disclosure of Interest:** L.B. Clayton: Employee of Norgine
R. Ng Kwet Shing: Employee of Norgine
C. Hassan: Has provided consultancy for Norgine.
All other authors have declared no conflicts of interest.

## P1267 HIGH MENTAL WORKLOAD EXPERIENCED DURING COLONOSCOPY IS ASSOCIATED WITH POOR ENDOSCOPIST PERFORMANCE

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**Introduction:** Studies have shown that there are a multitude of factors that affect the quality of colonoscopy. However, the effect of the endoscopist mental workload on their performance has been neglected. It is shown that health professionals exposed to excessive workloads and fatigue show degraded performance. The aim of this study was to measure the effect of mental workload as represented by the National Aeronautics and Space Administration-Task Load Index (NASA-TLX), on colonoscopic performance relative to the experience of the endoscopist and colonoscopy scheduling.
**Aims & Methods:** Procedures were observed prospectively in one institution for 3 groups; trainees, consultants and bowel cancer specialist programme (BCSP) endoscopists. On reaching the caecum the endoscopist marked on a validated pro-forma their corresponding workload on six subscales; mental demand, physical demand, temporal demand, effort, frustration and own performance, to generate a NASA-TLX score. Data on performance which included caecal intubation times (CIT), patient comfort and polyp detection rate (PDR) were noted. In addition, withdrawal times, time of day (am or pm) and queue order for procedures were recorded.
**Results:** A total of 202 procedures were undertaken between 6 endoscopists with a mean CIT of 9.2 minutes and PDR of 42%. Increasing mental workload was associated with increasing CIT ($r = 0.61$, $p = 0.07$) and inversely associated with withdrawal time ($r = -0.72$, $p = 0.03$). The mean mental workload during colonoscopy was lower in BCSP endoscopist v consultants v trainees (188 v 254 v 352 $p < 0.01$). On multivariate analysis, absence of polyp detection was associated with a procedure that was undertaken in pm with an above mean mental workload (OR 1.62, 95% CI 1.38–2.07) and withdrawal time of < 5 minutes (OR 1.53, 95% CI 1.32 – 1.91). Increased patient discomfort was associated with increased frustration on the subscale of the NASA-TLX score (OR 1.59, 95% 1.37 – 1.93) and being a trainee (OR 1.11, 95% 1.03 – 1.22). The use of ScopeGuide reduced the mental workload of consultants (227 v 282 $p < 0.01$), but not trainees or experts. Queue position had no impact on any of the markers of performance.
**Conclusion:** This study shows that high mental workload experienced during colonoscopy has a significant detrimental effect on the performance of endoscopists. Drop in PDR in pm procedures when only associated with high mental workload may explain some of the conflicting results of daily variations of PDR in other studies. Further studies are now required to look into measures that may reduce excessive mental workload.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1268 NARROW BAND IMAGING VERSUS WHITE LIGHT ENDOSCOPY IN THE CHARACTERIZATION OF RESIDUAL NEOPLASIA AFTER ENDOSCOPIC PIECEMEAL MUCOSAL RESECTION, A RANDOMIZED CONTROLLED TRIAL

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**Introduction:** Endoscopic Piecemeal Mucosal Resection (EPMR) of large or difficult sessile polyps in the colon is commonly used but it is associated with a recurrence of up to 25%. There is no evidence regarding whether Narrow Band Imaging (NBI) instead of High Definition White Light Endoscopy (WLE) could improve the detection of residual tumorat the follow-up after an EPMR polypectomy.
**Aims & Methods:** We conducted a randomized, controlled trial at our institution to assess the accuracy of NBI and WLE for the detection of residual neoplasia in the scar of a previous EPMR. (ClinicalTrials.gov, NCT02448693). During real-time colonoscopy, the same endoscopist evaluated the polypectomy scar using both techniques randomly (1:1) NBI-WLE or WLE-NBI. Any suspected neoplasia was classified independently by each technique as low/high confidence. An apparently normal scar was also evaluated and biopsied. The remainder of the colon was inspected as usual with WLE.
**Results:** A total of 120 lesions from 111 patients were included. Mean age was 67.8 yrs (SD:10.1); 57.5% males. Median size 20 mm (IQI:12–30); 80% right-sided. The mean time for scar review from initial resection was 4.8 months (SD: 1.8). Baseline characteristics were not different between groups (NBI-WLE or WLE-NBI). For each lesion, at most 3 biopsies were taken (total number of evaluated sites 142). NBI compared to WLE demonstrated an 87.8% vs 78.0% sensitivity, 85.1% vs 86.1% specificity and 85.9% vs 83.8% overall accuracy, respectively. This slight increase in sensitivity was not significant ($p = 0.125$). Regardless of the technique, 41/113 (36.3%) had neoplastic lesions on histologic assessment. Residual dysplasia was related at univariate analysis with size, body weight and Body Mass Index (BMI). In a multivariate analysis, polyp size ≥25 mm (OR 2.73, 95% CI: 1.15–6.47) and BMI ≥27kg/m$^2$ (OR 3.03, 95% CI: 1.34–6.89) were independently predictive factors of residual dysplasia, with and AUC of 0.69 (95% CI: 0.59–0.79).
**Conclusion:** NBI has a similar accuracy to WLE for residual dysplasia detection after EPMR. Patients with lesions over 25 mm have a high risk of residual neoplasia.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1269 COLD SNARE POLYPECTOMY MAY REDUCE DELAYED POSTPOLYPECTOMY BLEEDING COMPARED WITH CONVENTIONAL HOT POLYPECTOMY: A PROPENSITY SCORE-MATCHING ANALYSIS

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**Introduction:** Background and study aims: Cold snare polypectomy (CSP) for small colorectal polyps has lower incidence of adverse events, especially delayed post-polypectomy bleeding (DPPB). However, few data are available on comparisons of the incidence of DPPB of CSP and hot polypectomy (HP).
**Aims & Methods:** The aim of this study was to evaluate the incidence of DPPB after CSP and compare it with that of HP. A propensity score model was used as a secondary analysis. This was a retrospective cohort study conducted in a municipal hospital. We identified 539 patients with colorectal polyps from 2 mm to 11 mm in size who underwent CSP (804 polyps in 330 patients) or HP (530 polyps in 209 patients) between July 2013 and June 2015.
**Results:** There was no case of DPPB in the CSP group. Conversely, DPPB occurred in 4 patients (1.9%) after HP, resulting in a significant difference between the CSP and HP groups ($P = 0.025$). [KMD1] [t2] Propensity score-matching analysis created 402 matched pairs, yielding a higher DPPB rate in the HP group than CSP group ($P = 0.06$). However, significantly more patients in the CSP group had unclear horizontal margins that precluded assessment (83 vs 38 cases, $P < 0.001$). The retrieval failure rate was significantly higher in the CSP group than in the HP group (3% vs 0.7%, $P = 0.01$).
**Conclusion:** DPPB tended to be less frequent with CSP than HP, as selected by the propensity score-matching model; however, special care should be taken during polyp retrieval and horizontal margin assessment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1270 COLORECTAL SURVEILLANCE PROGRAM IN PORTUGUESE FAMILIES WITH LYNCH SYNDROME: A SINGLE-CENTRE COHORT STUDY

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**Introduction:** Lynch syndrome (LS) is associated with a high risk of colorectal cancer (CRC). Colonoscopy enables the identification and removal of adenomas or early cancers and is the mainstay of secondary prevention in LS patients.
**Aims & Methods:** To assess the cumulative risk for the development of colorectal adenomas and the prevalence of high-risk adenomas (HRA) or CRC during colonoscopic surveillance in LS. Single-centre cohort study; asymptomatic LS mutation carriers (MC) in a surveillance program (SP) between 2005–2015 were evaluated, with review of the colonoscopic reports (range 12–18 months). Patients with previous colectomy, who declined screening or received follow up in another hospital were excluded from the analysis. HRA were defined as $>=10$ mm, high-grade dysplasia or villous component. Statistics analysis: SPSS.V20.
**Results:** Among 331 MC, 184 were excluded from the study (previous colectomy: n = 130; declined screening: n = 8; surveillance in another hospital: n = 46). Therefore, 147 MC (from 73 families) were included (88 female/59 male), MLH1/MSH2/MSH6 mutations: 51/83/13. A total of 897 colonoscopies (mean 6.1 per person, range 1–13) were performed. In 161 colonoscopies (18%), 232 adenomas were detected. Adenomas were mainly found in the proximal colon (right colon-59.9%, left colon-29.8%, rectum-10.3%, $p < 0.001$). The cumulative risk of adenomas at 30, 40, 50 and 60 years of age was 6.2%, 20.5%, 34.2% and 43.8%, respectively, with a significantly positive correlation ($p = 0.002$). HRA or CRC were identified in 48 colonoscopies from 39 MC (26.5%); mean age was 49.4 years (24–80). Among these, 17/39 (43.6%) had HRA or CRC detected in the index colonoscopy. Eleven MC presented CRC (7.5%), right colon/left colon/rectum: 7/1/3; AJCC stage I/II/III: 8/1/2; four occurred at 12 (n = 2), 16 (n = 1) and 17 (n = 1) months from the previous colonoscopy and the remaining 7 were detected in the first screening colonoscopy or in the absence of compliance to the SP; no patient died from CRC.
**Conclusion:** Colonoscopic surveillance program in LS patients allowed the detection of adenomas in a large group of MC and adenoma cumulative risk increased steadily over the age range, as expected. Only 4/11 CRC occurred during regular surveillance protocol and most of them were diagnosed in early stages. These results validate an intensive SP in LS supporting that CRC-related mortality can be reduced.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1271 THE EFFICACY AND SAFETY OF ENDOSCOPIC MUCOSAL RESECTION WITH A CAP FOR RECTAL NEUROENDOCRINE TUMOR COMPARE TO ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Rectal neuroendocrine tumor (NET) are found incidentally during surveillance of colonoscopy. They can be resected using various endoscopic techniques.
**Aims & Methods:** The aim of this study is to compare efficacy of endoscopic mucosal resection with a cap (EMR-C) with those of endoscopic submucosal dissection (ESD) for rectal NETs. Methods: Between August 2006 and February 2016, 93 patients (93 lesions) underwent either EMR-C (n = 61) or ESD (n = 32) for rectal NETs at Gachon University Gil Medical Center. The endoscopic complete resection rate, procedure time, pathological complete resection, and procedure complications were analyzed retrospectively.
**Results:** Mean age was $49.7 \pm 10.6$ year in the EMR-C group and $50.3 \pm 11.5$ year in the ESD group. Mean tumor size was $4.63 \pm 2.40$ mm in the EMR-C group and $6.59 \pm 3.56$ mm in the ESD group. Endoscopic complete resection rate was 100% in both groups. Lateral margin involvement rate was significantly greater in the ESD group (25%) than in the EMR-C group (1.6%) ($P < 0.001$). The procedure time was significantly longer in the ESD group ($14.3 \pm 7.8$ min) than in the EMR-C group ($8.0 \pm 4.4$ min) ($P < 0.001$). Overall complication rate was not significantly different between the EMR-C group (4.9%) and the ESD group (15.6%).
**Conclusion:** Compared with ESD, EMR-C may be easy, simple, shorter and more effective procedure in removing rectal NETs. Therefore, EMR-C may be considered the treatment of choice for small rectal NETs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1272 LEVELS OF DIFFICULTY OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN THE WESTERN SETTING: STEPWISE EVALUATION OF PRE- AND INTRAOPERATIVE VARIABLES

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**Introduction:** The role of ESD in the therapeutic algorithm of the colorectal cancer as the less invasive approach to surgery to treat superficial neoplasms with a negligible risk of lymph node metastasis has been officially recognized in Japan and East Asia. Actually, its technical difficulty is an obstacle for its adoption and diffusion in the West, and the definitive identification of the prognostic variables of colorectal ESD difficulty would have important implications to improve ESD feasibility; promote its training and adoption.
**Aims & Methods:** Prospective study conducted in a nonacademic center by a single endoscopist with an experience of 60 colorectal ESDs. Inclusion criteria: colorectal neoplasms $\geq$15 or $\geq$20 mm with and without a scar of previous resection; no features of SM-deep invasion (Kudo pit pattern type V and Sano microcapillary pattern type 3B). ESD was performed by the standard technique. The ESD was defined as difficult if not en bloc and with an operating speed $>13$ min/cm$^2$ (threshold: 90 min for a 30-mm lesion). The prognostic role of preoperative and intraoperative variables was evaluated according to the neoplasm location in the rectum and colon. Operator experience was stratified in consecutive groups of 30 colorectal procedures.
**Results:** From 1.2012 to 7.2015, 140 ESDs were included: 110 (79%) in the colon, 30 (21%) in the rectum. Lesions had a median size 9cm$^2$ (range 1.2–33); were LST-G in 85 (61%); had a nodule $>20$ mm in 38 (27%), a scar in 31 (22%). Colonic neoplasms were significantly more frequently located on a semilunar fold ($P < .0001$). Rectal neoplasms had significantly more frequently a nodule $>$ 20mm ($P = .03$) and a scar ($P = .004$). Colonic ESDs were achieved with a higher en bloc resection rate (85%) and a lower difficulty rate (40%) than in the rectum (73% and 50%, respectively) with no statistical difference. Ineffective gravity counter traction was significantly more frequent in colonic ESD (22% vs. 3%; $P = .016$); SM fibrosis was significantly more frequent in rectal ESD (44% vs. 31%; $P = .045$). Preoperative variables of difficulty. In the rectum, the scar was the only prognostic variable (OR 12.3; $P = .03$). In the colon, prognostic variables were (in ascending order): operator experience $< 120$ procedures (OR 0.19; $P = .025$); size 7–12 cm$^2$ (OR 0.2; $P = .016$); sessile (OR 3.1; $P = .024$) and LST-NG (OR 10.5; $P < .005$) morphology; the scar (OR 12.7; $P = .038$). Intraoperative variables of difficulty. In the rectum, no variable was identified although severe SM fibrosis occurred only in difficult procedures. In the colon, prognostic variables were (in ascending order): perpendicular SM access (OR 5.1; $P = .042$); ineffective gravity counter traction (OR 12.3; $P = .002$); severe SM fibrosis (OR 21.9; $P = .010$).
**Conclusion:** This is the first study that evaluated the prognostic variables of colorectal ESD difficulty in the Western setting and demonstrated that there are qualitative differences according to the neoplasm location. The evaluation of the full spectrum of the preoperative and intraoperative variables confirmed that the level of ESD difficulty has to be evaluated on both the pre- and intraoperative variables. The combination of independent prognostic variables can be used to guide training and feasibility of ESD performed by Western endoscopists. Difficult neoplasms should be avoided until an expert level of competency has been achieved for easy neoplasms.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1273 ENDOSCOPIC MANAGEMENT OF LARGE RECTAL POLYPS

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**Introduction:** Since implementation of screening colonoscopy as primary method for the detection of early colorectal neoplasia in Germany many large ($>5$ cm in diameter) rectal lesions are found. Almost all of those are amenable to endoscopic resection via EMR or ESD.
**Aims & Methods:** We report our 3-year experience resecting those large rectal lesions endoscopically.
**Results:** Our patient cohort includes 46 patients (age 45–84 years) with rectal polyps from 5 to 11 cm in size. Some lesions spread in a circumferential

manner. All of those polyps were resected successfully after careful assessment using the Paris classification. EMR, ESD and hybrid methods were used. All procedures were performed on an outpatient basis. 4 patients did present with a post-polypectomy haemorrhage 24–72 hours after resection, which could be treated with endoscopic haemostasis (clips and APC). All patients were enrolled in an endoscopic surveillance program at 3–6 months after resection: 4 patients had evidence of polyp recurrence of up to 10 mm in diameter (all after piecemeal EMR). Repeat polypectomy did achieve complete histological resection.
**Conclusion:** Endoscopic resection of extensive rectal polyps is safe and effective on an outpatient basis. ESD is associated with a lower recurrence rate compared to piecemeal EMR. Post-interventional bleeding is quite frequent, but can be successfully managed endoscopically.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1274 THE DISCREPANCY IN PATHOLOGY RESULTS BETWEEN ENDOSCOPIC FORCEPS BIOPSY AND RESECTED SPECIMEN OF COLORECTAL POLYP

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**Introduction:** There are reports about discrepancy in results of histology between endoscopic forceps biopsy and resected specimens in gastric neoplasms. However, there are few studies in colorectum. The aims of this study were to investigate the decree of discordance in pathology result and to analyze the risk factors of underdiagnosis before complete removal co colorectal polyp.
**Aims & Methods:** Among 1171 patients who underwent endoscopic resection of colorectal polyp, 240 patients with pathology report prior to endoscopic resection were included in the study. We reviewed the medical records and endoscopic findings retrospectively and assessed the frequency and type of discordance in histology.
The baseline characteristics of the patients, morphology, size of the polyp and histology were compared between groups. Among the discordant group, risk factors of under-diagnosis were analyzed. Under diagnosis was defined as the cases when final pathology of total specimen showed more advanced type than those of biopsy specimen before resection.
**Results:** Mean age was 59.3 years and male to female ratio was 1:0.518 (158:82). Colorectal polyps were detected in the recto-sigmoid colon most frequently (53.75%). Mean size of the polyp was $18.5 \pm 9.8$ mm and 94.2% of them were removed by endoscopic mucosal resection. En-bloc resection rate was 97.9% and tubular adenoma with low-grade dysplasia was most common histology in 144 cases (58.8%). Change of the final histology after endoscopic resection was noted in 121 cases (50.4%). Among them, change to malignancy from benign after complete removal was noted in 25 cases (10.4%) and high-grade dysplasia to malignant was most common in 14 cases (5.8%). There noted under diagnosis in 80 (66.1%) and over-diagnosis was in 41 (33.9%). In under-diagnosis group, polyps above 10 mm in diameter and flat type morphology was significantly more common. By multivariate analysis, size above 10 mm was the only predictive factors of under- diagnosis after endoscopic resection.
**Conclusion:** The histology discrepancy between before and after endoscopic resection was noted in 50.4% of colorectal polyp and among them, 66.1% of them were under diagnosed nefore procedure. The rate was higher in flat morphology and increased with size increase. We need more attention for complete removal especially in case of larger than 10 mm flat type polyps.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1275 OPTICAL DETECTION OF COLORECTAL RESIDUAL NEOPLASIA AFTER ENDOSCOPIC MUCOSAL RESECTION WITH HIGH-DEFINITION WHITE LIGHT OR NARROW-BAND IMAGING COLONOSCOPY WITH OR WITHOUT NEAR-FOCUS: A PROSPECTIVE STUDY

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**Introduction:** Detection of subtle recurrences after colorectal endoscopic mucosal resection (EMR) is challenging. High-definition colonoscopy with narrow band imaging (NBI) and near-focus features may help in differentiating residual neoplasia from granular tissue and could thereby potentially reduce the need for pathologic assessment during EMR follow-up. The main objective is to evaluate the diagnostic value of high-definition white light and NBI with and without near-focus in the optical detection of residual neoplasia after EMR.
**Aims & Methods:** This multicenter prospective study started at one site in Florida in January 2016. Consecutive patients undergoing follow-up colonoscopy after a previous EMR of a ≥20 mm colorectal neoplasia were eligible for inclusion. Endoscopists predicted the presence of recurrence and their level of confidence (high or low) based on visual assessment of the previous EMR site with 1) high-definition white light colonoscopy without and 2) with near-focus, and 3) NBI without and 4) with near-focus. From each EMR-site tissue was obtained and histology, as reference standard, was assessed blinded to colonoscopy. A preliminary analysis was planned after enrollment of 50 patients. Negative predictive value (NPV), positive predictive value (PPV), sensitivity, specificity and diagnostic accuracy including 95% confidence intervals were calculated for all diagnostic modalities.
**Results:** Per-protocol analysis included 50 patients (males: n = 32 [64%], median age: 67 [range: 48–90] years) with 52 scar sites, with a median follow-up of 16 (range: 3–66) months. The prevalence of residual neoplasia was 37%. Diagnostic values for all EMR-scar sites and EMR-scar sites assessed with high confidence are summarized in table 1. The NPV of high confidence diagnosis was 100%, except for white-light (96%).

**Table:** Diagnostic value of optical detection of residual neoplasia during EMR follow-up.

| **All EMR-sites**, n = 52 | **White light** | **White light with near-focus** | **NBI** | **NBI with near-focus** |
|---|---|---|---|---|
| NPV | 97% [81–100] | 97% [81–100] | 97% [81–100] | 93% [76–99] |
| PPV | 86% [63–96] | 82% [59–94] | 82% [59–94] | 77% [54–91] |
| Sensitivity | 95% [72–100] | 95% [72–100] | 95% [72–100] | 89% [65–98] |
| Specificity | 91% [75–98] | 88% [71–96] | 88% [71–96] | 85% [67–94] |
| Accuracy | 92% [81–98] | 90% [78–96] | 90% [78–96] | 87% [74–94] |
| **High confidence diagnosis**, n (%) | 42 (81%) | 43 (83%) | 41 (79%) | 45 (87%) |
| NPV | 96% [80–100] | 100% [84–100] | 100% [84–100] | 100% [83–100] |
| PPV | 93% [64–100] | 88% [60–98] | 87% [58–98] | 80% [56–93] |
| Sensitivity | 93% [64–100] | 100% [73–100] | 100% [72–100] | 100% [76–100] |
| Specificity | 96% [80–100] | 93% [76–99] | 93% [75–99] | 86% [67–95] |
| Accuracy | 95% [83–99] | 95% [83–100] | 95% [82–99] | 91% [78–97] |

[.-.], 95%-confidence interval; n, number of EMR-sites.

**Conclusion:** These preliminary results suggest a very high NPV and good PPV for the optical diagnosis of residual neoplasia with NBI with near-focus when assessed with high confidence, in a setting with a surprisingly high residual neoplasia rate. These advanced imaging modalities may improve real-time decision making in follow-up after colorectal EMR, particularly the avoidance of biopsy.
**Disclosure of Interest:** M.B. Wallace: Dr. Michael Wallace reports consulting income from iLUmen and Interscope and grant support from Boston Scientific, Olympus, Medtronic and Cosmo pharmaceuticals.
All other authors have declared no conflicts of interest.

## P1276 ACCURACY OF COLORECTAL POLYP SIZE ESTIMATION BY ENDOSCOPY

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**Introduction:** The size of colonic polyps affects postpolypectomy surveillance interval, 3 years if ≥10 mm, and the implementation of strategies based on real-time histological diagnosis, in those < 6 mm.
**Aims & Methods:** The aim of the study was to assess overestimation and underestimation of the endoscopic size (ES) compared to histological size (HS) of colon polyps, in cutoffs of 5and 10 mm, and associated factors. Prospective consecutive outpatient colonoscopies of single endoscopist (May 2014 - November 2015). Only polyps resected in toto with ES and HS available with single fragment in a single pot. Logistic regression analysis to assess factors associated with the over/underestimation of HS, reference method, with ES (dichotomized ≤5 vs >5 mm and ≥10 vs <10 mm); OR (95%CI).
**Results:** In 511, of the 720 colonoscopies, ≥1 polyp was resected. 52.37% (961/1835) of resected polyps were excluded by the absence of valid HS; factors associated with the exclusion were age (y) OR 1.015(1.003–1.028); non 0-Ip morphology, 0-Is OR 3.717(2.007–6.884) and 0-II OR 3.866(2.098–7.121); and resection with forceps OR 4.763(3.822 - 5.936). 874 polyps were included, of 375 colonoscopies, ES Md 5 mm (ICR 3–8): 62.57% <6 mm, 25.3% 6–9 mm and 12% ≥10 mm. HS Md 4 mm (ICR 3–6); 79.1% (691/874) adenomas and 20.9% (183/874) hyperplastic/serrated lesions. 19.05% (20/105) with ES ≥10 mm were overcalled; non screening (iFOBT) indication OR 4.687(1.352–16.255) and proximal to splenic flexure localization OR 6.715(1.741–25.902).

3.25% (25/769) with ES <10 mm were undercalled; female OR 2.082(0.902–4.803) and non 0-II morphology, 0-Is OR 3.89(1.524–9.933) and 0-Ip OR 11.543(3.424–38.913). 34.4% (112/326) with ES ≥6 mm were overcalled, 3 villous component; suboptimal bowell cleaning OR 2.662(1.224–5.79); non 0-Ip morphology, 0-Is OR 4.296(1.861–9.917) and 0-II OR 5.259(2.095–13.201); and proximal to splenic flexure localization OR 1.726(0.968–3.077). 8.39% (46/548) with ES <6 mm were undercalled, null advanced histology; non screening (iFOBT) indication OR 4.141(1.598–10.73); and non 0-II morphology, 0-Ip OR 3.035(0.328–28.123) and 0-Is OR 2.216(1.177 - 4.174). 42 colonoscopies show ≥1 polyp with ES and HS discordance in 10 mm cutoff, 45 polyps. Posptpolypectomy surveillance changed in 0.3% (11/375) of the included colonoscopies: 10 to 3 years in five and 3 to 10 years in six.
**Conclusion:** In colorrectal polyps ES overestimation, compared to HS, is greater than the underestimation, cutoffs of 5 and 10 mm. The clinical relevance is residual in the postpolypectomy surveillance, but it can affect the impact of policies of discard and resect polyps <6 mm.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1277 ANALYSIS OF COLONOSCOPY TO CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD) PATIENTS

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**Introduction:** There have been several case reports on peritonitis following colonoscopy in continuous ambulatory peritoneal dialysis (CAPD) patients. Then antibiotic prophylaxis for patients undergoing colonoscopy while on CAPD is recommended. And, in general, colonoscopy in patients with peritoneal adhesion is considered to be difficult. However, whether CAPD is risk factor for complications or incomplete study of colonoscopy is unclear. We conducted a study to investigate preparation, difficulty and complication of colonoscopy to CAPD patients on the basis of single-center experience in Japan.
**Aims & Methods:** 52 CAPD patients were enrolled. They underwent 93 colonoscopies between August 1982 and October 2015. Demographic and clinical data, use of antibiotics before colonoscopy, preparation status, difficulty of intubation, procedure performed and complication were retrospectively analyzed. Preparation was evaluated by Aronchick scale (1: excellent – 5: inadequate). These patients were then compared with a control group with normal renal function matched 2:1. For statistical analysis, $\chi^2$ or Fisher's exact test was used.
**Results:** In 93 colonoscopy procedures to CAPD patients, prophylactic antibiotics were given in 11. Regarding colon preparation quality, 13% of colonoscopies were judged poor or inadequate. Average intubation time was 16.8 ± 13.5 mins and cecal intubation rate was 94%. No post-operative complication was observed. Aronchick scale was higher in CAPD patients (2.5 ± 1.1 in CAPD group vs 1.8 ± 0.7 in control group, $p < 0.001$). Longer intubation time (16.8 ± 13.5 in CAPD group vs 10.6 ± 8.2 in control group, $p = 0.005$) and lower cecal intubation rate (94% in CAPD group vs 100% in control group, $p = 0.042$) were observed in CAPD group. Colonoscopists felt difficulty more occasionally in procedures for CAPD patient (35% in CAPD group vs 15% in control group, $p = 0.010$).

| Patient Characteristics | CAPD Group (N = 52) | Control Group (N = 104) | p Value |
|---|---|---|---|
| Age | 64.1 ± 9.4 | 65.6 ± 11.9 | 0.422 |
| Male sex, n (%) | 35 (67) | 69 (66) | 0.717 |
| BMI, kg/m$^2$ | 21.3 ± 3.0 | 22.2 ± 3.1 | 0.073 |
| Inpatient status, n (%) | 23 (44) | 46 (44) | 1.000 |
| Indication for colonoscopy, n (%) | | | |
| History of polyps | 7 (13) | 33 (32) | 0.014 |
| Fecal occult blood positive | 12 (23) | 21 (20) | 0.678 |
| Rectal breeding | 10 (19) | 13 (12) | 0.264 |
| Diarrhea | 3 (6) | 5 (5) | 0.797 |
| Anemia | 8 (15) | 8 (8) | 0.136 |
| Constipation | 0 (0) | 4 (4) | 0.152 |
| Other | 12 (23) | 20 (19) | 0.315 |
| Patient background, n (%) | | | |
| Coronary artery disease | 15 (29) | 25 (24) | 0.420 |
| Cirrhosis | 2 (4) | 5 (5) | 0.785 |
| COPD | 0(0) | 0(0) | - |
| Stroke | 9 (17) | 16 (15) | 0.758 |
| Diabetes | 13 (25) | 29 (28) | 0.771 |
| Diverticulitis | 3 (6) | 3 (3) | 0.377 |
| Hypertension | 34 (65) | 50 (48) | 0.036 |
| Thyroid disorder | 3 (6) | 2 (2) | 0.199 |
| Tricyclic antidepressants use | 0 (0) | 2 (2) | 0.314 |
| History of colonic or pelvic surgery | 18 (35) | 42 (40) | 0.457 |
| Preparation | | | |
| Aronchick scale, 1(excellent) - 5(inadequate) | 2.5 ± 1.1 | 1.8 ± 0.7 | <0.001 |
| Colonoscopy's difficulty | | | |
| Intubation time, min | 16.8 ± 13.5 | 10.6 ± 8.2 | 0.005 |
| Colonoscopy to the cecum, n (%) | 49 (94) | 104 (100) | 0.042 |
| Colonoscopists feel difficulty, n (%) | 18 (35) | 16(15) | 0.010 |
| adenoma detection, n (%) | 14 (27) | 23 (22) | 0.464 |
| Biopsy, n (%) | 6(12) | 16(15) | 0.515 |
| Polypectomny, n (%) | 15(29) | 32(31) | 0.805 |
| Senior colonoscopists, n (%) | 18 (35) | 37 (36) | 0.967 |
| Post-operative complications, n (%) | 0 (0) | 0 (0) | - |

**Conclusion:** We found CAPD was associated with insufficient preparation and difficult intubation of colonoscopy. No complication after colonoscopy was observed either in patients with or without prophylactic antibiotics. In our study, we cannot demonstrate a necessity of prophylactic antibiotics in colonoscopy for CAPD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1278 TRACTION ASSISTED COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION USING CLIP AND LINE: A FEASIBILITY STUDY

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**Introduction:** Colorectal endoscopic submucosal dissection (C-ESD) is a challenging procedure because it is often difficult to maintain good visualization of the submucosal layer. To facilitate C-ESD, we designed a novel traction method, namely "Traction assisted C-ESD using clip and line (TAC-ESD)", and investigated its feasibility.
**Aims & Methods:** We retrospectively analyzed 67 patients with large colorectal superficial lesions who had undergone TAC-ESD between October 2014 and July 2015. The main outcome was the procedural success rate of TAC-ESD, which we defined as successful, sustained application of clip and line to the lesion until the end of the procedure. TAC-ESD was performed as follows. Before the colonoscope was inserted, a polyester line was inserted into its accessory channel by grasping the line with hemostatic forceps, and pulling it up through the working channel. Then we tied the ends of the line together outside the colonoscope. After that, the colonoscope was inserted as usual and the actual C-ESD procedure started. After submucosal injection, the mucosa was incised on the anal side of the lesion. Next, the line was cut externally at the hand control end of the colonoscope and the accessory channel end of the line tied to the teeth of the clip attached to an applicator. At this stage, it was important not to fully open the clip. The clip and line were then retracted into the applicator and the applicator inserted into the accessory channel. The clip was fully opened in the colon and used to grasp the anal side of the specimen, after which the line was pulled gently by hand to provide good visibility of the submucosal layer. Finally, the submucosal layer was dissected easily under direct visualization [1,2]. In the rectum, TAC-ESD was performed as follows. First, a polyester line was tied to the teeth of a clip, which was attached to an applicator. The clip and line was then retracted into the applicator as in preparation. Next, the colonoscope was inserted into the rectum. After a mucosal incision on the anal side of the lesion was performed, the colonoscope was withdrawn outside of the rectum. The applicator was inserted into the accessory channel of the colonoscope, and the line was pulled back up through the working channel. Then, the colonoscope was reinserted into the rectum. The clip was fully opened within the rectum and used to grasp the anal side of the lesion. Since then, the procedure was same as above [3].
**Results:** Study subjects were 34 men and 33 women with a median age of 70 years (range 41–89 years). Forty-six (69%) lesions were located in the proximal colon, 11 (16%) in the distal colon, and 10 (15%) in the rectum. Thirty-four (50%) lesions were a granular type of laterally spreading tumor. The median lesion size was 27 mm (range 14–125 mm). The median resected specimen size was 34 mm (range 20–135 mm). The overall median procedure time was 64 min (range, 18–291 min). The clip and line was successfully attached to the lesion in all cases, thus good visibility of the submucosal layer was obtained in all cases in the initial part of TAC-ESD. However, in seven cases, the clip and line detached from lesion during submucosal dissection, all of which were in the proximal and the procedure times over 70 minutes. Therefore, the procedural success rate of TAC-ESD was 90% (60/67). En bloc resections of all lesions were achieved and R0 resections confirmed in 61/67 lesions (91%). Intra-procedual perforation occurred in two lesions (2.9%) and was treated successfully with endoscopic clipping. There were no fatal adverse events.

**Conclusion:** TAC-ESD is feasible and safe for C-ESD and may improve the ease of performing C-ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1279 SHOULD WE RECOMMEND A LIQUID DIET OR A LOW FIBER DIET THE DAY BEFORE A SCREENING COLONOSCOPY? NON-INFERIORITY RANDOMISED CLINICAL TRIAL


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**Introduction:** Current clinical guidelines do not favor a specific diet the day before a screening colonoscopy. Participants in a screening program are usually healthy and motivated patients who comply adequately with instructions; on the other hand good tolerability is very important in asymptomatic participants to improve adherence to surveillance colonoscopies.
**Aims & Methods:** Main objective: to compare the efficacy of a low-fiber diet (LFD) versus liquid diet (LD) the day before a screening colonoscopy. - Secondary objectives: to compare the adenoma detection rate (ADR) and tolerability. This is a randomized controlled clinical trial to show non-inferiority of LFD versus LD. 276 participants of the colorectal cancer screening program in Barcelona came for a personal interview to schedule the colonoscopy date and to receive instructions on bowel preparation and were randomized to LFD or LD. Both groups were given 4 liters of poliethylenglicol in split fashion. The main outcome measure was inadequate bowel preparation measured with the Boston Bowel Preparation Scale (<2 points in any segment). The endoscopists were blinded for the diet received. The sample size was calculated estimating 4% of inadequate bowel preparation with LD (our previous data) with a differential of 6%, to keep inadequate bowel preparation <10%. The patients were given questionnaires on tolerability and acceptability to be filled during the bowel preparation. Analogic visual scale was used.
**Results:** 276 consented patients were randomized from January to June 2015 (3% nonappearance) and 267 patients fulfilled the protocol. 132 were included in LD and 135 in LFD, both groups were similar in baseline variables. Inadequate bowel preparation was 6.8% (95% CI: 3.6%-12.5%) for liquid diet and 2.2% (95% CI: 0.8%-6.3%) for LFD ($p = 0.07$). ADR was 53% for LD and 60% for LFD ($p = 0.3$). LDF participants referred less hunger ($p = 0.006$) and less perception of excessive volume of laxative ($p = 0.04$), without differences in bloating or nausea. Acceptability was 85% (LD) and 88% (LFD), $p = 0.6$.
**Conclusion:** The efficacy of a screening colonoscopy following a low fiber diet is excellent, with less than 10% of inadequate bowel preparations. It also improves hunger and perception of excessive volume. This study shows that low fiber diet is the ideal dietary recommendation for the day before a screening colonoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1280 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): ADOPTION AND OUTCOME OF POCKET CREATION METHOD IN A TERTIARY CENTRE IN SINGAPORE


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**Introduction:** A retrospective review of a single centre's adoption of pocket creation method in colorectal ESD.
**Aims & Methods:** Patients' records from all colorectal ESD cases performed in our institution were selected from June 2014 to January 2016. A total of 55 colonic ESD cases were performed and nine cases were excluded as they were deem unsuitable on examination.
**Results:** A total of 46 patients underwent colonic ESD in which the average age was 68.4(47–85). 22 cases were done via pocket creation method and 24 via hybrid/others. 12 out of 22 cases achieved complete en bloc resection whereas the remaining 10 cases required endoscopic piecemeal resection (EPMR). The complication rate of the pocket creation method was 4.6% (1/22) versus the hybrid group 8.3% (2/24). The size of the lesion resected in the pocket creation method ranged from 23–60 mm x 20–55 mm with the largest en bloc resection specimen at 60 mm x 55 mm x 7 mm.
**Conclusion:** Overall pocket creation method is safe, effective and facilitates submucosal dissection to achieve en bloc resection of colonic lesions. Safety and success rates can be improved via development of new strategies, training system and equipment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1281 LONG FOLLOW UP AFTER ENDOSCOPIC RESECTION OF COLORECTAL CARCINOMA WITH SUBMUCOSAL INVASION: RESULTS OF A MONOCENTRIC RETROSPECTIVE STUDY


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**Introduction:** Little is known about the long-term outcome of early colorectal cancer with submucosal invasion following endoscopic resection. The present study addressed determine the long-term outcome of endoscopically resected sm+ colorectal cancer.
**Aims & Methods:** Aim of this monocentric retrospective study was to evaluate the follow-up of patients after endoscopic resection of colorectal carcinoma with submucosal invasion Patients who benefits of an endoscopic resection (ER) of a submucosal invasive colorectal carcinoma between 2006 and 2012, were included in this study. Submucosal invasion was stratified using the Paris classification1 (sm1, $sm^2$, sm3). If the exact depth of submucosal invasion couldn't be assessed on the specimen, lesion was stratified as "smX". Complementary surgical resection was purposed if the submucosal invasion was either superior to 1000$\mu$m or inferior to 1000$\mu$m with poor prognosis criteria (budding, low differentiation, lympho-vascular invasion). In another situation, clinical and endoscopic follow-up was recommended.
**Results:** Forty-one patients (16 female, mean age = 30 yrs [35–88] were treated endoscopically for 43 submucosal invasive colorectal carcinomas (rectum = 17, colon = 26). Endoscopic mucosal resection was performed in 35 cases (81.5%), submucosal dissection in 5 (11.5%) or hybrid technique in 3 (7%). Mean diameter was 30 mm (10–50 mm). ER was macroscopically complete in all cases, en-bloc in 51%. Morbidity was 14% (bleeding = 4, perforation = 2), treated conservatively in all cases. Histology showed well or moderately differentiated carcinoma in respectively 49% and 35% (7 missing datas). Budding, lymphatic or vascular invasion were identified respectively in 5%, 11% and 2%. Deep margin was superior to 1 mm in 58% of cases. Lateral margin was clear in 77% after en-bloc resection (unevaluable after piecemeal resection). Submucosal invasion was stratified sm1, $sm^2$, sm3 or smX respectively in 32%, 28%, 5% or 35%. Follow up after ER was obtained in 29 patients (71%). Surgical resection was performed for 11 patients (4 $sm^2$, 6 smx, 1 sm1 with budding), 9 patients being followed (surgical contraindication or refusal). None residual adenomatous tissue was found on the surgical specimen in all patients operated, but 2 patients with early rectal cancer were N+. Definitive classification of patients treated surgically was: pT0N0 = 9, pT0N1 = 1, pT0N2 = 1. No metastasis occurred during a median follow up of 48 months [12–84 m]. Eighteen patients were included in a follow-up program for a mean duration of 54 months [12–96 m]: sm1 = 8, sm1 with budding = 1, $sm^2 = 3$, sm3 = 1, smx = 5. Local recurrence occurred in 1 patient but was treated endoscopically. No metastasis occurred during follow up.
**Conclusion:** ER is an efficient and safe treatment for submucosal invasive colorectal adenocarcinoma without high risk criteria. Local recurrence is spare and most often treatable endoscopically. Clear margins of the resected site on endoscopic examination seems superior to microscopic analysis of lateral margins to predict complete resection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1283 DETECTION OF THE DESMOPLASTIC REACTION USING ENDOCYTOSCOPY: A NOVEL DIAGNOSTIC MARKER OF SUBMUCOSAL OR DEEPER INVASIONS IN COLORECTAL CARCINOMA

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**Introduction:** Desmoplastic reaction (DR), characterized by stromal myofibroblast infiltration of the tumor, is thought to initiate in response to the invasion of carcinoma cells into the submucosal (SM) or deeper layers. DR expression increases as cancer invades, hence immerging to the surface of cancer. Reports in the past have shown that the presence of DR in the surface of early colorectal cancer suggests deep invasion into the submucosa. Therefore, the pathological determination of a DR in colorectal carcinoma is useful for predicting massive submucosal invasion.However, no previous study have reported in vivo assessment of DR using EC thus far. We have recently demonstrated that some submucosal invasive colon cancer represents fine granular structure (FGS) on endocytoscopy (EC) (not published).
**Aims & Methods:** The aim of this study was to determine the usefulness of EC in detecting DR. From May 2005 to August 2013, 72 lesions were diagnosed at our institution as EC3b according to the EC classification[(1)], suggesting submucosal or deeper invasion. For judging DR, these lesions were diagnosed by single pathologist. Pathological definition of DR were as follows: 1) the presence of carcinoma is required for the detection of DR; 2) a DR involves an area of collagen fiber accumulation and myofibroblast proliferation; 3) carcinoma and inflammatory infiltration does not signify the presence of DR; and 4) histological findings were determined by HE staining alone[(2)].FGS on EC was defined as granular aggregate formed by round nuclei which are smaller than cancer nuclei. We hypothesized that FG represents inflammatory cell and myofibroblast cell infiltration. The area with FGS on EC were pathologically examined in hematoxylin and eosin-stained specimen. We calculated positive ratio of FGS among subject lesions and overall accuracy of the identification of FGS on EC.
**Results:** Among the 72 lesions, 26 were positive for FGS, and 88.5% of the lesions (23/26,) had a DR. The overall accuracy of FGS on EC that was predictive of a DR was 86.1% (table1).

**Table 1:** Correlation between the presence of FGS and a superficial exposing desmoplastic reaction.

| | DR (+) | DR (-) | total |
|---|---|---|---|
| **FGS (+)** | 23 | 3 | 26 |
| **FGS (-)** | 7 | 39 | 46 |
| **total** | 30 | 42 | 72 |

N = 72; DR, desmoplastic reaction; FGS, fine granular structure

**Conclusion:** In conclusion, the presence of FGS in EC may be useful for predicting the presence of a DR, suggesting the clinical usefulness of EC in informing treatment for colon cancer with SM invasion.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1284 APPROPRIATENESS OF ANTIBIOTIC PROPHYLAXIS AND NOVEL RISK FACTORS FOR POST ERCP BACTEREMIA - REAL LIFE EXPERIENCE OF A HIGH VOLUME CENTER

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**Introduction:** According to current recommendations[1] antibiotic prophylaxis is not recommended when an ERCP is likely to achieve complete biliary drainage. However, clinically significant post-ERCP bacteremia (PEB) occurs in up to 5% of cases and other risk factors are not fully established.
**Aims & Methods:** The aim of this study was to evaluate specific risk factors for PEB. This was a retrospective cohort study of 1.082 consecutive ERCP procedures performed in the Tel-Aviv Medical Center between January 2012 - December 2013. Exclusion criteria: a) age < 18 years; b) positive bacterial blood culture before ERCP; c) scheduled full antibiotic treatment prior to ERCP; d) hospitalization > 14 days before ERCP and e) missing critical data. Stepwise Logistic Regression analysis and Decision Tree algorithms were used for prediction modeling of PEB.
**Results:** A total of 626 ERCPs performed in 434 patients were included. Mean age- 66.49 ± 15.4 years and male:female ratio 46.5%/53.5%. The rate of clinically significant PEB was 3.7% (23/626). The bacteria cultured were: Enterobacteriaceae (1.8%), Extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (1.3%), Pseudomonas aeruginosa (0.3%) and Acinetobacter baumannii (0.3%). In a case by case review by a blinded endoscopist, antibiotic prophylaxis was administrated in 22.2% of the cases but was indicated only in 7%. Prophylaxis was not indicated in any of the PEB cases. Demographic and procedure characteristics were comparable between the PEB and non-PEB groups except for ERCP duration (PEB 40.87 ± 42.7 min vs. non-PEB 28.64 ± 24.3 min, P = 0.02) and the prevalence of tandem EUS/ERCP (PEB 21.7% vs. non-PEB 6.6%, P = 0.006). In a stepwise multivariate logistic regression (ROC 0.716), only 3 variables were included: Tandem EUS/ERCP (Yes vs. No)(OR 3.563, P = 0.027); ERCP duration (minutes)(OR 1.009, P = 0.132) and Age at ERCP (years)(OR 1.031, P = 0.063 borderline significance). In a decision tree model (ROC 0.741) only two cut points were included: duration of the ERCP > 61.5 minutes (PEB probability of 12%) and age > 74.5 years (PEB probability of 6.5%).
**Conclusion:** In a retrospective point of view, antibiotic prophylaxis according to current guidelines was not indicated in any of the cases that resulted in PEB. Moreover, prophylaxis was not indicated in 60% of the cases it was actually administrated, but the prevalence of PEB was similar to previous reports. Thus, better classification of risk factors is required. In our study, ERCP duration over 1 hour, Tandem EUS – ERCP and age above 75 years were found to be significant risk factors for PEB. These factors should be further evaluated as indications for prophylactic antibiotic treatment before ERCP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1285 MINIMAL ENDOSCOPIC SPHINCTEROTOMY PLUS LARGE BALLOON DILATION FOR EXTRACTION OF LARGE STONES IN PATIENTS WITH PERI-AMPULLARY DIVERTICULA

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**Introduction:** Stone extraction represents the most frequent reason for performing endoscopic retrograde cholangiopancreatography (ERCP). Since its introduction in 1974 endoscopic sphincterotomy (ES) has been widely considered the choice technique for biliary duct stones removal [1]. Although its universal use, several complications can be caused by ES [2]. In 2003 Ersoz et al. introduced the technique of dilation assisted stone extraction (DASE), consisting of an EPBLD following a limited ES [3]. DASE has been proven to be safe and effective for extraction of large CBD stones, with some evidences of reduced post-procedure complication rates and need for mechanical lithotripsy when compared to ES [4].
**Aims & Methods:** Aim of our study is to evaluate efficacy and safety of DASE for the extraction of large biliary stones in patients with PAD. All patients with evidence of biliary large stones and concomitant peri-ampullary diverticula from 4 Italian ERCP referral centers undergoing a therapeutic ERCP were enrolled in our study. All ERCPs were performed by experienced endoscopists at high volume centers (> 200 ERCPs per year). Peri-ampullary diverticula were classified into three types based on the location of the major papilla with respect to diverticula: type 1, when papilla was located inside the diverticulum; type 2, when papilla was located on the perimeter of the diverticulum; and type 3, when papilla was located towards 1 cm outside the diverticulum. All data concerning procedure and during and post-procedural complications were recorded.
**Results:** A total of 81 patients (36 males and 45 females, median age 75 years old - range, 45 to 93 years old) were enrolled in our study. Follow-up average time was 363 days (92–734 days). A deep biliary cannulation was reached in 78/80 patients (biliary cannulation rate 97.5%). Pancreatic main duct was cannulated in 16/80 patients (pancreatic cannulation rate 20%). A prophylactic pancreatic stent was placed in 3 cases. A successful stone removal was achieved in 74/78 patients (94.8%). Mechanical lithotripsy was successfully used in 2/78 patients (2.6%). An unsuccessful extraction was observed in 5.2% of patients. In all but one papilla was located into the diverticulum (PAD1), in about 50% of patients there were three or more stones, with a maximum diameter of about 20 mm. Two of four unsuccessful patients experienced a complication. A total of 7 complications were observed, of which one mild bleeding during procedure. Post-

procedural complications were 2 mild bleeding, both on anticoagulants within 72 h before (2.5%), 4 mild pancreatitis (5%) and 1 severe perforation (1.2%). Univariate and multivariate analyses of complications for predictors (see table 3 and 4) showed that age, location of stones and stone extraction success were significantly associated with complications ($p < 0.05$). In consideration of the small number of patients referring to hospitals with concomitance evidence of large biliary stones and PAD, sample size presented in our series can be considered statistically adequate for a descriptive analysis for this group of patients.
**Conclusion:** Results from our study show that DASE can be considered a safe technique to obtain a successful removal of large biliary stones. Moreover, DASE can be considered the first choice technique in patients with concomitant evidence of large biliary stones and PAD, avoiding use of ML and reducing risks of biliary bacterial contaminations.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1286 A MULTI-CENTER RETROSPECTIVE STUDY ON THE CLINICAL VALUE OF TWO GENERATIONS OF A SINGLE-OPERATOR CHOLANGIOSCOPE: ANALYSIS OF 239 CONSECUTIVE APPLICATIONS


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**Introduction:** Cholangioscopy provides direct visualization of the biliary tract by using ultra-slim endoscopes that can be introduced into the bile duct. The SpyGlass system is a catheter-based technology which can be used for diagnostic and therapeutic purposes by a single operator. Recently, a new generation of this technology has been launched.
**Aims & Methods:** This retrospective study aimed to evaluate the clinical value of SpyGlass cholangioscopy by analyzing consecutive examinations at nine Austrian referral centers for bilio-pancreatic endoscopy. Patients characteristics, indications, image quality from 1 (bad) to 10 (optimal) and outcome were assessed and compared between two SpyGlass generations (SpyGlass Legacy and SpyGlass DS).
**Results:** Over a ten-year period 239 consecutive examinations (161 Legacy, 78 DS) were performed in 205 patients (125 male, 80 female, median age 71 years, range 25–95 years). The main indication was evaluation of indeterminate strictures (68%), followed by cholangiolithiasis (24%). Prior to SpyGlass examinations, a majority of patients (84%) had already undergone a median number of 1 conventional ERCP examinations (range 1 – 10) with inconclusive or insufficient result. In 76% of stricture cases targeted biopsies were taken using the SpyBite biopsy forceps which had a diagnostic accuracy (according to the further clinical course) of 80%. In 85% of stone cases lithotripsy by targeting an endohydraulic or laser probe was successful (57% complete, 28% partial stone resolution). Image quality was rated 4 in median for the Legacy system and 8 in median for the DS system ($p = 0.02$, Fisher's exact test).
**Conclusion:** In this multi-center retrospective analysis cholangioscopy using the SpyGlass system was very effective for diagnosis and therapy of biliary disease. Image quality was rated much better for the new system, potentially resulting in an even higher diagnostic yield in the future.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1287 ENDOSCOPIC THERAPY FOR BILE LEAKS AFTER LIVER TRANSPLANTATION: AN ANALYSIS OF TWO HIGH-VOLUME TRANSPLANT CENTERS


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**Introduction:** Bile leak after liver transplantation (LT) is commonly treated with endoscopic retrograde cholangiopancreatography (ERCP); however, there is scarce data in regard to the optimal strategy with this technique. We aimed to examine the role of ERCP in LT recipients with bile leaks at two large institutions.
**Aims & Methods:** We reviewed all ERCPs performed in LT recipients with bile leak and duct-to-duct biliary anastomosis at two high-volume transplant centers (Hospital Clinic-Barcelona and Mayo Clinic-Rochester) from 2003 to 2015. Information on clinical and endoscopic outcome was obtained from electronic health records and endoscopy databases from both institutions. Preoperative and endoscopic variables were evaluated as factors determining outcomes after ERCP.
**Results:** A total of 80 patients were included (45-Hospital Clinic and 35–Mayo Clinic). Location of bile leak was: anastomotic (45%), T-tube (34%), intrahepatic (10%), cystic remnant (9%) and cut surface (2%). Forty-seven (59%) patients underwent ERCP with plastic stent placement and 33 patients (41%) underwent sphincterotomy alone. Complete resolution was obtained in 94% of the stent group vs. 58% of the sphincterotomy group ($p = 0.01$). Resolution occurred in <3 months in 76% of the stent group vs. 37% of the sphincterotomy group ($p = 0.01$). There was no difference in 3-month survival among both groups. Percutaneous transhepatic therapy and surgery were required in 4% and 6%, respectively in the stent group vs. 12% and 42% respectively in the sphincterotomy group ($p = 0.22$ and $p < 0.001$ respectively). The only predictive factor of bile leak resolution was stent placement. Complications of ERCP occurred in 10% (5 mild pancreatitis, 3 mild bleeding).
**Conclusion:** ERCP is a safe and effective therapy for post-LT bile leaks. Combination therapy with sphincterotomy and plastic stent is highly successful and more effective than sphincterotomy alone. These results indicate that ERCP with sphincterotomy and plastic stent placement should be considered the treatment of choice for bile leaks in LT recipients with duct-to-duct biliary anastomosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1288 CAN ULTRASLIM UPPER ENDOSCOPE REPLACE FIVEROPTIC CHOLEDOCHOSCOPE FOR PERCUTANEOUS TRANSHEPATIC CHOLANGIOSCOPY?: A FEASIBILITY STUDY


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**Introduction:** PTCS is useful for evaluation of indeterminate biliary stricture and management of intrahepatic bile duct stone. PTCS using fiberoptic choledochoscopeis limited by unsatisfactory image quality and fragility.
**Aims & Methods:** The aim of this study was to evaluate the feasibility of an ultraslim upper endoscope during PTCS. A total of 16 patients with biliary stricture and/or intrahepatic bile duct stone were included prospectively. All the patients underwent PTCS with ultraslim upper endoscope (distal end outer diameter 5.4 mm, working channel 2–2.2 mm, total working length 110 cm) after by fiberoptic choledochoscope. Primary outcome was technical success, defined as advancement of the ultraslim upper endoscope into the target site. Secondary outcomes were adverse events, quality of image, and success rates of diagnostic and therapeutic intervention.

**Results:** The PTCS using ultraslim upper endoscope was completed in 16 of 16 patients (13 biliary strictures, 3 intrahepatic bile duct stones). NBI observation with targeted biopsy was successfully performed in 9 of 13 patients with biliary strictures. The overall diagnostic accuracy of histologic sampling was 77.8% (2 malignancy, 5 benign). Technical success of lithotripsy was achieved in 3 of 3 (100%) procedures. No adverse event including air embolism and cholangitis was ovserved.
**Conclusion:** PTCS using an ultraslim upper endoscope is feasible and useful for evaluation of biliary stricture and managment of bile duct stone instead of fiber-optic choledochoscope.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1289 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) FOR THE ELDERLY AND EXTREMELY ELDERLY: DOES AGE REALLY MATTER?


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**Introduction:** The role of endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis and treatment of biliary diseases is well established. Despite the aging population, few studies have evaluated its efficacy and safety in elderly patients.
**Aims & Methods:** Our aim was to assess ERCP safety and effectiveness in elderly patients and to identify predicting factors for a successful ERCP in the considered patient group. Clinical data from patients >85 years-old that underwent ERCP in our centre during a two years period was retrospectively analyzed. Elderly patients were defined by being 85–90 years-old and extremely elderly by being >90 years-old. Variables analyzed included demographics, comorbidities, ERCP indications, final diagnosis and immediate and delayed complications (within 30 days of the exam).
**Results:** Our sample included 108 patients, 43 (39.8%) male and 65 (60.2%) female, with a mean age of 89 years (85–103). A total of 147 duodenoscopies were performed (98 in elderly and 49 in extremely elderly patients). ERCP indication was suspected lithiasis (25.9%), obstructive jaundice (24.5%), cholangitis (22.4%), acute pancreatitis (12.9%), stent placement/replacement/removal (10.2%) or other (4.1%). Most frequent diagnosis were lithiasis (61.2%) and neoplastic stenosis (27.9%), with 8.5% of normal exams. There was a 93% cannulation rate, in 15.5% of cases after precut papillotomy or double-wire technique. Juxtapapillary duodenal diverticula were identified in 20.4% of patients. Regarding therapeutic procedures performed, there were 62.8% of sphyncterotomies, 8.8% of precut papillotomies, 8.5% of ballon sphincteroplasties, 58.1% of stone removal, 34.9% of biliary stent placements (64% of which plastic) and 7.8% of prophylactic pancreatic duct stent placements. Immediate complications were identified in 7.7% of patients, namely bleeding (9 cases) and bradycardia (1 case). Gastrointestinal bleeding episodes were mild, without hemodynamic repercussion, effectively managed endoscopically and with only one case needing subsequent transfusion. Delayed complications (analyzed in 99 patients with 30 days follow-up), identified in 2% of patients, with 1 case of cholangitis and 1 case of gastrointestinal perforation (treated endoscopically). There were no cases of post-ERCP pancreatitis. Mortality during the 30 days follow-up occurred in 4 patients (4%), with only 1 case due to the procedure (cholangitis/sepsis). There was an association between cannulation rate and the presence of juxtapapillary duodenal diverticula (20% of no cannulation if present vs 3.7% in the remaining cases, $p = 0.002$). There was an association between immediate bleeding and precut execution (44% in patients with precut vs 3.3% in the remaining, $p < 0.001$), but not to previous antiplatelet or anticoagulant therapy (5.4% in medicated patients vs 6.9% in the remaining, $p = 0.771$). No statistical difference was identified regarding immediate (7.1% vs 6.1%, $p = 0.817$) or delayed (1.5% vs 9.1%, $p = 0.071$) complication rates for the two considered age groups.
**Conclusion:** In our sample, ERCP was safe and effective in both elderly and extremely elderly patients. The presence of juxtapapillary diverticula was a negative predicting factor for a successful exam, whereas precut execution was a predicting factor for immediate bleeding. Age and previous treatment with antiplatelet or anticoagulant agents were not associated to an increased risk of complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1290 EFFICACY OF ENDOSCOPIC GALLBLADDER STENTING IN ACUTE CHOLECYSTITIS


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**Introduction:** Laparoscopic cholecystectomy is recommended for acute cholecystitis. However, in our hospital, cholecystectomy is performed 2–3 months after presentation, only after the gallbladder inflammation has resolved. Cholecystectomy is occasionally not possible in high-risk elderly patients with comorbidities. Although percutaneous gallbladder drainage (PTGBD) is usually considered an alternative to cholecystectomy, endoscopic gallbladder stenting (EGBS) has recently been shown to be useful.
**Aims & Methods:** We aimed to evaluate the efficacy of EGBS as either a bridge to surgery (BTS) for cholecystectomy or as a permanent placement.We retrospectively studied 35 EGBS procedures performed at our hospital between April 2012 and April 2016. In total, 31 patients (18 men and 13 women; mean age, 72 years [range, 41–88 years]) underwent EGBS, with a 5Fr single pig-tail stent with a thread. The main outcome measure of this study was the efficacy of EGBS.
**Results:** EGBS was performed for BTS in 19 cases and permanent placement in 12 cases. The overall EGBS technical success rate was 88.6%. Clinical success was noted in all the cases wherein technical success was achieved with the EGBS procedure. However, there were 3 cases of recurrence. The mean placement duration was 77 days (range, 23–290 days) in the BTS group and 348 days (range, 6–874 days) in the permanent stent placement group. Complications included damage of the cystic duct ($n = 1$) and pancreatitis ($n = 1$).
**Conclusion:** EGBS can improve quality of life, and may be effective for patients who are poor surgical candidates or those requiring a BTS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1291 THE USEFULNESS OF ARGON PLASMA COAGULATION ABLATION SUBSEQUENT TO ENDOSCOPIC SNARE PAPILLECTOMY FOR AMPULLARY ADENOMA


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**Introduction:** Endoscopic snare papillectomy (ESP) of major papilla is safe and effective alternative to surgical resection of ampullary adenoma. Argon plasma coagulation (APC) is widely used in ESP as adjuvant method to control bleeding and to ablate residual tumor. However, the safety and effectiveness of subsequent APC ablation during ESP are not fully evaluated. The aim of this study is to evaluate the short-term and long-term outcomes of APC ablation as adjuvant method during ESP.
**Aims & Methods:** The data of patients who had undergone ESP for ampullary adenoma between September 2005 and August 2015 were restrospectively reviewed.
**Results:** The 100 patients underwent ESP for ampullary adenoma with curative intent. The mean patient age was $57 \pm 11$ years old and 70 (70.0%) patients were male. The mean tumor size was $1.63 \pm 0.80$ cm. After ESP, adjuvant APC ablation was performed in 53 (53.0%) patients. There were no significant differences in procedure-related adverse events including pancreatitis (ESP + APC vs. ESP alone; 5.7% vs. 14.9%, $p = 0.183$), cholangitis (ESP + APC vs. ESP alone; 1.9% vs. 10.6%, $p = 0.096$), or perforation (ESP + APC vs. ESP alone; 1.6% vs. 2.1%, $p = 1.000$). However, bleeding events occurred less frequently after APC ablation (ESP + APC vs. ESP alone; 5.7% vs. 21.3%, odds ratio = 0.222, $p < 0.05$). During follow-up period (mean $931 \pm 881$ days), papillary stricture (ESP + APC vs. ESP alone; 9.4% vs. 4.3%, $p = 0.442$) and recurrence rate (ESP + APC vs. ESP alone; 20.8% vs. 23.4%, $p = 0.750$) were not significantly different.
**Conclusion:** During ESP procedure, additional APC ablation may have beneficial effect in decreasing bleeding events.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1292 ETOMIDATE WITH MEPERIDINE VS MIDAZOLAM WITH MEPERIDINE FOR SEDATION DURING ENDODSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAM (ERCP): A SINGLE CENTER, RANDOMIZED CONTROLLED, SINGLE BLINDED STUDY


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**Introduction:** Endoscopic retrograde cholangiopancreaticography (ERCP) is a crucial technique for specific pancreatobiliary diseases. Maintaining adequate sedation is vital to achieve successful outcome.
**Aims & Methods:** The objective of this study was to compare the efficacy and adverse effects of sedating patients undergoing ERCP with etomidate (ETM) with those of midazolam (MDZ).This was single-institute, prospective, randomized single blinded study. In the MDZ group, the initial dose of MDZ was 0.06 mg/kg with 50 mg of meperidine (MPD), after which 1 mg was added intermittently during ERCP. In the ETM group, 0.1 mg/kg ETM was initially injected with 50 mg of MPD, and an additional dose of 2 mg was added if needed.

**Results:** Of 63 patients undergoing ERCP, 33 and 30 were randomly allocated to the MDZ and the ETM group, respectively. In the ETM with MPD arm, the intervention rates were significantly lower (number of intervention, $p < 0.01$), the satisfaction scores of patients and the endoscopists were significantly higher ($p = 0.015$ and $p < 0.01$, respectively), and there were fewer hypoxic events ($p = 0.013$).
**Conclusion:** We concluded that ETM in combination with MPD is superior to MDZ with MPD for sedating patients during ERCP. Therefore, endoscopists can consider ETM with MPD as a good sedative regimen for therapeutic ERCP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1293 RISK FACTORS FOR THE RELAPSE OF POST-LIVING DONOR LIVER TRANSPLANTATION (LDLT) BILIARY STRICTURE AFTER ENDOSCOPIC TREATMENT


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**Introduction:** Although endoscopic management is useful to treat Post-LDLT anastomotic stricture, the recurrence of the biliary stricture sometimes happen after removal of biliary stricture.
**Aims & Methods:** The aim of our study is to evaluate the risk factors related to recurrence of Post-LDLT biliary stricture. 1106 patients underwent LDLT between May 1996 and May 2014 at Samsung Medical Center (Seoul, Korea). 241 of these patients who were clinically suspected of developing biliary stricture underwent ERCP and 145 of them were performed ERBD successfully. Among the 241, 22 patients were showed normal cholangiogram or minimal stricture which didn't need for ERBD. We followed up the 145 ERBD group for more than 12 months. Among 145 who were performed successful ERBD, 11 were expired, 34 were maintained ERBD due to persistent biliary stricture, and 94 could remove the ERBD stent due to improvement of biliary stricture. 6 persons could remove ERBD also, but they were followed less than 12 months. Among the 94 patients of ERBD removal group, 69 were maintained ERBD removal state, but 20 showed biliary stricture recurrence. 5 recurred below the 3 months, and 20 were recurred after 3 months from time to remove the ERBD. In order to identify the predictors of recurrent biliary stricture after ERBD removal, we analyzed donor factors, recipient factors, surgical factors, endoscopic procedure-related factors, and cholangiography-related factors.
**Results:** The success rate for the endoscopic management of biliary strictures after LDLT was 66.2% (145 of 219 patients), and recurrence rate of the biliary stricture was 21.3% (20 of 94 patients). The recurrence of the biliary stricture was more frequent in patients with in the case of Non-B, Non-C liver cirrhosis, and the elderly age of the donor ($p < 0.05$).
**Conclusion:** At the time to consider the removal of ERBD after endoscopic treatment of post-LDLT anastomotic stricture, we should be careful when the patients have the risk factors for the relapse of biliary stricture.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1294 THE USEFULNESS OF DIRECT PERORAL CHOLANGIOSCOPY COMBINING WITH INTRADUCTAL ULTRASONOGRAPHY FOR THE EVALUATION OF INDETERMINATE BILE DUCT LESIONS


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**Introduction:** The evaluation of indeterminate bile duct strictures or filling defects is clinical challenging. Direct peroral cholangioscopy (DPOC) may be helpful by allowing endoscopic visualization and targeting biopsy. However, the evaluation of bile duct wall layers or extraductal lesions is impossible with DPOC. Intraductal ultrasonography (IDUS) provides high-resolutional ultrasonic findings of the bile duct wall and extraductal structures.
**Aims & Methods:** We evaluated the usefulness of DPOC combining with IDUS in evaluation of indeterminate bile duct lesions. Total 31 patients with indeterminate biliary strictures or undefined filling defects in preceding conventional imaging modalities including ERCP were evaluated by IDUS and DPOC by using an ultra-slim upper endoscope. Inclusion criteria includes dilated distal bile duct more than 8 mm. Asymmetrical irregular wall thickening and intraductal protruding or polypoid lesions with ductal disruption in IDUS findings were diagnosed as malignant lesions. Irregular surface with stricture, tortuous tumor vessels, protruding mass lesions, and granular or papillary mucosal lesions in DPOC findings were diagnosed as malignant lesions. Final diagnoses were confirmed by histopathologic results and/or clinical follow-up outcomes.
**Results:** Evaluated indeterminated bile duct lesions were finally diagnosed as 17 malignant, 1 adenoma and 13 benign lesions. The overall diagnostic accuracy of DPOC visual impression for indeterminate bile duct lesions was 80.6% (25/31). Three nonspecific small polypoid lesions and one flat elevated lesion without dilated vessels or mucosal irregularity in DPOC had been diagnosed as polypoid masses with ductal wall thickening with or without invasion in IDUS. One papillary mucosal lesion in DPOC was showed as symmetrical wall thickening in IDUS. And one intraductal polypoid mass lesion in DPOC was revealed as extraductal invading mass in IDUS. DPOC-guided targeted biopsy was performed in 87.1% (27/31) with diagnostic accuracy of 92.6% (25/27).
**Conclusion:** DPOC with targeted biopsy was useful for differentiating indeterminate bile duct lesions with high diagnostic accuracy. IDUS may provide adjunctive information before performing cholangioscopic evaluation by providing bile duct wall and periductal images of target lesions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1295 RISK FACTORS AND PROPHYLAXIS OF POST ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PANCREATITIS


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**Introduction:** The pancreatitis that happens after an Endoscopic retrograde cholangiopancreatography (ERCP) is still the most frequent complication of this procedure. This post ERCP pancreatitis (PEP) remains an event that can potentially cause considerable harm to the patient.
**Aims & Methods:** The main objective was to study prospectively the risk factors associated with this complication by defining their impact in this condition. We also aimed to evaluate the efficacy of the standard prophylactic methods used to prevent PEP. Methods: we designed a form to collect patient and procedure data from each ERCP executed in the endoscopic unit of a Gastroenterology department. It was registered the duration and number of attempts to catheterize the Vater papilla, execution of needle-knife precut, catheterization of the Wirsung with and without contrast injection, septotomy (trans-pancreatic sphincterotomy) pneumatic dilation and the application of pancreatic protection stents and rectal indomethacin. The patient was followed-up during, at least, 24 hours after the procedure. PEP was defined as

acute onset or increasing intensity abdominal pain that persisted more than 24 hours after ERCP and was associated with increase in amylase and/or lipase more than 3 times the normal cut-off value. The severity of PEP was defined according to the Atlanta 2012 classification. Statistics were done with SPSS v. 20 (SPSS v. 20 Inc., IBM, Chicago IL).
**Results:** In 12 months we prospectively enrolled 329 patients. Then 56 patients were excluded because of incomplete follow-up. Out of the 273 finally included 52.7% were women. Mean age 70 ± 15 years (20 to 95). The PEP rate was 5.9% corresponding to 16 cases. Only 2 were considered severe pancreatitis (one death from those 2 patients). The remaining were all mild pancreatitis. Prophylactic administration of rectal indomethacin was done in 77% cases. It wasn't used in cases of simple/very low risk procedures and in patients with contraindication. In the 16 patients with PEP only one didn't receive indomethacin. None of the risk factors considered revealed correlation with pancreatitis or odds ratio statistically significant for higher risk. The utilization of pancreatic stent (5.9% cases) didn't correlate with lower pancreatitis risk. Whenever septotomy was performed (4.4%) PEP didn't occur (no statistical significance). All the executants had large experience on this procedure and there were no differences in the PEP rate among them.
**Conclusion:** Even with indomethacin prophylaxis there's always a risk of PEP occurrence related to the procedure. This risk can only be partially reduced. We cannot draw conclusions about any of the risk factors. Probably there are also some individual patient related risk factors that make pancreatitis more likely in some patients. Those should be the subject of future studies. Prophylaxis with intensive hydration should also be tested in large clinical trials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1296 SAFETY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR PATIENTS TAKING ANTITHROMBOTIC AGENTS

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**Introduction:** In 2012, the Japan Gastroenterological Endoscopy Society published guidelines for the management of gastrointestinal endoscopy for patients using antithrombotic agents. The guidelines were created from the viewpoint of bleeding risk during continuation of antithrombotic agents, as well as thromboembolic risk related to periprocedural interruption of antithrombotic agents. In Japan, there has recently been an increase in the number of patients taking antithrombotic agents who require endoscopic retrograde cholangiopancreatography (ERCP). The aim of this study was to evaluate the safety of ERCP for patients taking antithrombotic agents.
**Aims & Methods:** We retrospectively investigated the records of patients who received ERCP between April 2015 and March 2016 in our institution. Among 320 patients, 70 had taken antithrombotic agents (14 anticoagulant agents, 55 antiplatelet agents, and 1 both agents) (group A), and 250 patients had not taken any antithrombotic agents (group N). We compared the background and treatment outcome between the two groups.
**Results:** Patients in group A were older than those in group N [79.0 (52–93) vs. 72.0 (20–97) years, median (range), $p < 0.001$]. There were no significant differences in sex (group A vs. group N; male 51.4% vs. 60.0%) and causes (biliary stone 41.4% vs. 38.4%, pancreatic cancer 22.9% vs. 27.2%, and biliary tract cancer 21.4% vs. 20.4%). There was a significant difference between the two groups in comorbidity (ischemic heart disease or arrhythmia 22.9% vs. 0.8%, and ischemic brain disease 14.3% vs. 0.4%, $p < 0.001$). Regarding treatment, there were no significant differences in the implementation of endoscopic sphincterotomy (EST) (48.6% vs. 37.2%), and the use of rectal diclofenac (74.3% vs. 68.0%). Regarding complications, there were no significant differences in bleeding after ERCP (2.9% vs. 1.6%), post-ERCP pancreatitis (4.3% vs. 4.8%), and perforation (1.4% vs. 0.8%). Antithrombotic agents were interrupted in nine of 14 (64.3%) patients taking anticoagulant agents, 28 of 55 (50.9%) patients taking antiplatelet agents, and one patient taking both agents. In group A, one of two patients who had bleeding after EST continued taking anticoagulant agents. There were no thromboembolic events during interruption of antithrombotic agents.
**Conclusion:** This retrospective study showed the safety of ERCP for patients taking antithrombotic drugs. However, one should always consider the bleeding risk of the procedure and the risk of thromboembolic events related to discontinuation of antithrombotic agents, especially for procedures with a high risk of bleeding, such as EST.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1297 A PERSONALIZED TREATMENT OF GASTROINTESTINAL STROMAL TUMORS IS ENABLED BY ANALYZING ENDOSCOPIC ULTRASOUND-GUIDED BIOPSIES: A PROSPECTIVE, TEN-YEAR COHORT STUDY

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**Introduction:** Gastrointestinal stromal tumors (GIST) are challenging to diagnose preoperatively and the diagnostic sensitivity of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is reported as non-satisfactory. Moreover, accurate information on the tumor mutation profile and on the tumor proliferation rate is important prior to treatment of patients with GIST. The genotype driven targeted therapy with imatinib is highly effective but should be prescribed exclusively to patients carrying tumors with sensitive mutations.
**Aims & Methods:** The aims of this study were to diagnose and characterize GISTs by the use of endoscopic ultrasound (EUS) and to evaluate the tumor response to neoadjuvant treatment. All GIST-patients punctured by EUS in the tertiary center of West Sweden were prospectively and consecutively included between 2006–2015. Fine-needle aspiration (EUS-FNA) was performed in 2006–2011. In 2012–2015 EUS-FNA and an additional fine-needle biopsy (EUS-FNB) were performed on the same lesions according to a randomized protocol. The FNB-biopsies were subjected to Sanger-sequencing of KIT and PDGFRA. The Ki-67-index of the FNB-biopsies ($Ki\text{-}67_{EUS}$) and the resection specimens ($Ki\text{-}67_{SURG}$) was determined.
**Results:** In sixty-four patients included the diagnostic accuracy increased from 50% (EUS-FNA) to 98% (EUS-FNB), $p < 0.001$. Sequencing was successful in 43/44 (98%) of the cases (KIT-mutation 73%, PDGFRA-mutation 18%, wild-type 7%) with full mutation congruence comparing EUS-biopsies with resected specimens. In patients not treated with neoadjuvant imatinib, the $Ki\text{-}67_{EUS}$ was at equal level as the $Ki\text{-}67_{SURG}$, 2.7% vs 2.9%, $p = 0.68$. In treated patients carrying sensitive mutations, the $Ki\text{-}67_{EUS}$ was significantly higher than the $Ki\text{-}67_{SURG}$, 2.5% vs 0.2% $p = 0.005$ with a significant reduction of the Ki-67-index = -91.5% (95% CI: -82.4 – -96.0), $p = 0.005$.
**Conclusion:** A diagnostic and prognostic pretreatment tumor characterization in GIST-patients is achievable by the analysis of EUS-fine needle biopsies. Such a characterization may guide the initiation of imatinib and allows evaluating tumor response to neoadjuvant therapy. EUS should be considered early in the management of GIST to enable a personalized treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1298 EUS-GUIDED CYST-ENTEROSTOMY USING A SELF-EXPANDING METAL STENT IS A MORE COST-EFFECTIVE STRATEGY FOR THE TREATMENT OF PANCREATIC FLUID COLLECTIONS

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**Introduction:** EUS-guided cyst-enterostomy (EUS-CE) has become the mainstay for endoscopic treatment of symptomatic pancreatic fluid collections (PFCs). The traditional approach (Approach I) of inserting multiple double-pigtail plastic stents with sequential dilation of the tract with or without naso-cystic irrigation is successful but requires repeated endoscopic intervention. The comparative effectiveness of newer approaches utilizing a fully covered expandable metal stent (FCEMS, Approach II) is not understood very well.
**Aims & Methods:** Our aim is to compare the clinical efficacy and cost impact of these approaches in the management of PFCs. We included all patients that underwent EUS-CE for PFCs. Clinical efficacy was defined as symptomatic improvement and cyst resolution on cross-sectional imaging. Follow-up was until stent removal. The total cost was calculated for each EUS-CE (including anesthesia and radiology costs), all subsequent procedures and hospital length of stay (HLOS).
**Results:** Between November 2010 and March 2016, 12 patients underwent Approach I and 16 patients underwent Approach II. Patients in Approach I had a mean of 3.9 endoscopic interventions (range 1–8), mean procedure time of 72 min (range 43–130 min) and 11.4 days of HLOS (range 0–33 days) compared with 1 endoscopic intervention, mean procedure time of 39 min (range 16–65 min) and 2.2 days HLOS (range 0–7 days) in Approach II ($p = 0.001$, $p = 0.01$ and $p = 0.02$, respectively). Cyst resolution was documented in 12/12 patients with a mean follow-up of 284 days in Approach I (range 86–628 days) and 15/16 patients with a mean follow-up of 98 days in Approach II (range 1–239 days). There were 6 adverse events in Approach I compared with 2 in Approach II ($p = 0.03$). The average cost of Approach I was $17,590 compared with $6,165 for Approach II ($p = 0.01$).
**Conclusion:** Despite the increased upfront cost of a metal stent, the use of a FCEMS for EUS-CE in the treatment of PFCs is effective, safe and results in significant overall cost savings by reducing the number of endoscopic re-interventions and HLOS.
**Disclosure of Interest:** G.S. Sandha: I am a consultant and medical advisory board member for Boston Scientific Inc.
All other authors have declared no conflicts of interest.

## P1299 AN INTERNATIONAL MULTICENTER STUDY COMPARING EUS-GUIDED PANCREATIC DUCT DRAINAGE WITH ENTEROSCOPY-ASSISTED ENDOSCOPIC RETROGRADE PANCREATOGRAPHY FOLLOWING WHIPPLE SURGERY

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**Introduction:** Endoscopic management of post-Whipple pancreatic complications with enteroscopy-assisted endoscopic retrograde pancreatography (e-ERP) is associated with high failure rates. EUS guided-pancreatic duct drainage (EUS-PDD) has shown promising results; however, there have been no comparative data looking at these two modalities.
**Aims & Methods:** The goal of this study is to compare EUS-PDD with e-ERP in terms of technical success (PDD through dilation/stent), clinical success (improvement/resolution of pancreatic-type symptoms) and adverse event (AE) rates in patients with post-Whipple anatomy. This is an international multicenter comparative retrospective study at 7 tertiary centers (2 US, 2 European, 2 Asian, and 1 South American). All consecutive patients who underwent EUS-PDD or e-ERP between 1/2010 - 8/2015 were included.
**Results:** 66 patients (mean age 57, 48% female) and 75 procedures were identified with 40 in EUS-PDD and 35 in e-ERP. Technical success was achieved in 92.5% procedures in EUS-PDD compared to 20% procedures in e-ERP (OR49.3, $p < 0.001$). Clinical success (entire cohort) was attained in 87.5% procedures in EUS-PDD group compared to 17% in e-ERP (OR33.8, $p < 0.001$). AEs occurred more commonly in EUS-PDD group (35% vs. 2.9%, $p < 0.001$). However, all complications were rated as mild or moderate. Procedure time and length of stay was not significantly different between the two groups. On multivariable analysis, EUS-PDD was independently associated with increased rate of clinical success and adverse events.
**Conclusion:** EUS-PDD is superior to enteroscopy-ERP in post-Whipple anatomy in terms of efficacy with acceptable safety. As such, EUS-PDD should be considered as a potential first-line treatment in post-pancreaticoduodenectomy anatomy.
**Disclosure of Interest:** T. Moreels: Received free Olympus equipment for procedures
M. Khashab: Consultant for Boston Scientific
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## P1300 IMPACT OF THE FORMATION OF A REGIONAL EUS INTEREST GROUP AMONGST COMMUNITY HOSPITALS ON THE YIELD OF EUS GUIDED TISSUE ACQUISITION IN SUSPECTED PANCREATIC MALIGNANCY

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**Introduction:** The use of EUS-guided tissue acquisition (TA) in diagnosing pancreatic malignancy has increased throughout the past two decades. Data on the diagnostic accuracy of this technique have almost exclusively been generated in tertiary referral centers. To our knowledge no data are available on role and quality of EUS guided TA in diagnosing pancreatic malignancy in community hospitals i.e. in general gastroenterology practice neither regarding ways to potentially improve its diagnostic yield.
**Aims & Methods:** To determine quality of EUS-guided TA in diagnosing pancreatic malignancy in community hospitals, in particular after the formation of a regional EUS group interactively discussing cases, techniques and outcomes on a regular basis. First, we retrospectively analysed the yield of 143 EUS-guided TA procedures for suspected pancreatic malignancies from 7 different hospitals in the southwestern part of the Netherlands before the regional EUS interest group was established. Next, after initiating the regional EUS interest group and after having had several meetings discussing cases and the specifics of various EUS-FNA/FNB techniques, we prospectively recorded data on EUS-guided TA procedures from January to October 2015 in 5 of these hospitals. Patient characteristics, size and localization of the pancreatic mass, EUS-characteristics of the mass, size and type of needles, use of suction techniques, number of needle passes, and types of cytology medium for cellblock were recorded. Outcome measures were the results of histo-, and cytopathological analysis, which were compared to a gold standard of 6 months follow-up and histopathology from resected tissue and/or metastatic tissue (1). The results of the first 75 prospective cases were compared to the retrospective data using chi-square and Mann-Whitney U tests when appropriate.
**Results:** Both the increase in procedures diagnostic for malignancy and decrease in procedures yielding insufficient material for diagnosis were significant ($p < 0.05$). Sensitivity, specificity, PPV, NPV and diagnostic accuracy in the retrospective cohort were: 65%, 100%, 100%, 44%, and 72% respectively. In the prospective cohort sensitivity, specificity, PPV, NPV and diagnostic accuracy were: 86%, 100%, 100%, 50%, and 88%. Significant differences between retrospective and prospective series were: the number of needle passes, the use of suction techniques and needle size. In the prospective series less 19 G needles were used, and both more needle passes and more suction were applied. Both groups were comparable with regards to age, gender and final histopathological diagnosis.
**Conclusion:** The establishment of a collaborative regional EUS group with ongoing case reviews and discussions on technical aspects of EUS guided TA has led to a statistically and clinically significant improvement of diagnosing pancreatic cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1301 CLINICAL ROLE OF FORWARD VIEWING ECHOENDOSCOPE FOR EUS-FNA, ESPECIALLY "SUCTION METHOD WITH CAP" FOR EUS-FNA OF SUBMUCOSAL TUMORS

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**Introduction:** Endoscopic Ultrasonography-guided Fine-Needle Aspiration (EUS-FNA) has become a dispensable examination in the clinical fields. Generally Oblique-viewing echoendoscope (OVE) has been employed for EUS-FNA and has elevator and long hard tip, which results in less pushability and less maneuverability. Recently Olympus Medical Systems (Tokyo) has launched a new forward-viewing echoendoscope (FVE). We have investigated its usefulness and limitation of FVE for not only therapeutic EUS but also diagnostic EUS-FNA, especially sucusion method with cap for EUS-FNA of submucosdal tumor.
**Aims & Methods:** We have perfomed 111 cases (averaged 60 y/o, M:F- = 61:49) of EUS-FNA, which includes 37 pancreas tumors etc. 35 submucosal lesions, 10 lymph adenopathy, 3 others and 26 therapuetic EUS-FNA (13 pseudocyst drainage, 9 EUS-biliary drainage, 3 EUS-pancreatic duct drainage, and 1 CPN,) up to now. The specification of FVE is as follows, maximum size of its tip is 14.2 mm in diameter, channel is 3.7 mm in diameter, and 90 degree of ultrasonographic field without elevator and balloon. In case of submucosal tumor, we have used "suction method", in which cap has been attached to the echoendoscope and we are keeping suction during EUS-FNA procedure. Then we have investigated its usefulness and limitation.
**Results:** The image quality and penetration of FVE is nearly of the same as conventional OVE such as GIF-UCT260. Its sampling rate is 88.2% (75/85) and diagnostic rate is also 87.1% (74/85). We had got 85% (17/20) accuracy in submucosal tumors less than 3 cm with "suction method". for EUS-FNA of submucosal tumor. Concerning about therapuetic EUS-FNA, it is rather easy to perform pseudocyst drainage, biliary drainage, and pancreatic duct drainage. Because using FVE, it is easy to puncture the gastrointestinal wall vertically, then it makes good pushability. And we have experienced a strictured case of anastomosis after Child's operation, in which we directly inserted FVE like a enteroscope, and punctured dilated intrahepatic bile duct and inserted metallic stent. We have successfully treated 100% (13/13) for pseudocyst drainage, 88.9% (8/9) for EUS-BD, 100% (3/3) for EUS-PD, 100% (1/1) for EUS-CPN with FVE. Finally We have leakage complications (EUS-BD).
**Conclusion:** We concluded that new FVE is useful not only for therapuetic EUS-FNA but also for diagnostic EUS-FNA, especially "suction method with cap" is useful for EUS-FNA of submucosal tumors.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1302 EFFICIENCY OF STYLET CAPILLARY SUCTION AND STANDARD SUCTION TECHNIQUE OF ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION (EUS-FNA) IN SOLID PANCREATIC CANCER

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**Introduction:** Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is recommended as the first-line sampling procedure for the histological/cytological diagnosis of solid pancreatic cancer. Currently, there are no evidence-based guidelines about the detailed methods of sampling and processing of samples, therefore, they vary substantially across medical centers.
**Aims & Methods:** To compare the diagnostic yield of EUS-FNA samples obtained with stylet capillary suction technique or with standard suction using a 5 mL syringe based on the classification of Papanicolau Association in 75 prospectively enrolled patients with solid pancreatic masses. The number of diagnostic samples, cellularity and bloodiness were assessed, and considering the result of study, we established a recommendation for sampling.
**Results:** EUS-FNA sampling resulted diagnostic samples in 58 of 75 cases (77.33%): with standard suction in 57 cases (76.00%) and with capillary suction in 52 cases (76.33%). Technical success rate (100% vs. 93.33%) and the number of samples were significantly higher in the standard suction group (1.87 vs. 3.5; $p < 0.001$). Although, there was no difference in the cellularity (1.75 vs. 1.52; $p = 0.2556$), the blood contamination of samples obtained by standard suction was substantially increased (1.57 vs. 2.33; $p < 0.001$), which made the pathological diagnosis difficult, therefore the rate of diagnostic samples was lower (47.36% vs. 33.23%; $p = 0.003$). The cytological examination of fluid obtained by flushing the needle with saline was diagnostic in 29 cases (38.67%). In 40 cases histological samples were obtained, in 22 cases with both of the two techniques, in 11 cases only with capillary suction and in 7 cases only with standard suction. Histological samples were diagnostic in two third of the cases (67.50%). The diagnostic yield of EUS-FNA sampling was not influenced by the needle type, tumor size and location.
**Conclusion:** Both capillary and standard suction are effective in the EUS-FNA sampling of solid pancreatic masses. Due to higher negative pressure, standard suction is recommended in case of fibrotic pancreatic cancer, but the increased bloodiness of vascularized tumors decreases the diagnostic yield of sampling.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1303 CHOLEDOCHOLITHIASIS AND COMMON BILE DUCT ECTASIA: ALWAYS ASSOCIATED?

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**Introduction:** The diagnosis of choledocholithiasis by abdominal ultrasound (US) has low sensitivity. However, its accuracy for the detection of common bile duct (CBD) ectasia is higher, and the presence of this surrogate finding contributes to the diagnosis of choledocholithiasis. Furthermore, endoscopic ultrasound (EUS), providing high resolution imaging, has significantly improved the understanding of the relationship between the presence of lithiasis and CBD dilation, irrespective of their dimensions.
**Aims & Methods:** We aimed to evaluate and characterize by EUS the presence of CBD dilation on a population of patients with choledocholithiasis. Methods: Retrospective analysis of the EUS procedures done in a single centre over a five-year period. The patients with choledocholithiasis on EUS were selected, and the ones with biliary tract neoplasia or biliopancreatic stents in place excluded. CBD dilation was considered when the calibre measured just above the stone was higher than 6 mm or 8 mm in patients without gallbladder.
**Results:** 109 EUS procedures were selected. Female sex 63.3% (n = 69); average age of 68.06 years (24–96); average number of stones present 2.4 ± 1.5, average size of 7.7 ± 4.4 mm; stone with diameter < 5 mm in 57.8% (n = 63); diameter between 5 and 10 mm in 26.6% (n = 29) and diameter > 10 mm in 15.6% (n = 17). CBD dilation confirmed in 65.1% (n = 71) of patients; with an average CBD diameter of 10.2 ± 4.4 mm. 25.7% (n = 28) of patients had no gallbladder; from the remaining, 22.9% (n = 25) had cholecystitis and 93.6% (n = 74) had evidence of biliary sludge or gallbladder stones. There was a statistical association between the presence of CBD dilation and sex (more males without ectasia) and with the size of the endoluminal stones. Nevertheless there was no association with age, number of stones, previous cholecystectomy, cholecystitis or presence of gallbladder stones.
**Conclusion:** On the population of our study, 34.9% (n = 38) of the patients with choledocholithiasis showed no CBD dilation. These findings support the indication for EUS when CBD lithiasis is suspected, mainly if there is no biliary tract dilation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1304 ENDOSCOPIC ULTRASOUND (EUS) GUIDED CYANOACRYLATE INJECTION FOR VARICEAL OBTURATION AS SECONDARY PROPHYLAXIS FOR PATIENTS AT HIGH RISK FOR RECURRENT GASTROESOPHAGEAL VARICEAL BLEEDING: A PILOT STUDY

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**Introduction:** Patients with hepatocellular carcinoma (HCC) and/or portal vein thrombosis (PVT) are at higher risk for recurrent variceal bleeding and worse clinical outcome. Prior studies reported a rebleeding rate of 28%–42% in patients with HCC and oesophageal variceal bleeding treated with endoscopic cyanoacrylate (CYA) injection or band ligation. Recent evidence suggested prophylaxis against rebleeding may improve outcomes in patients with HCC. However, the optimal approach for secondary prophylaxis in such patients has not been well defined. The utility of endoscopic ultrasound (EUS)-guided CYA injection for variceal obturation in these high-risk patients has not been studied.
**Aims & Methods:** This is a prospective pilot study evaluating EUS-guided CYA injection for variceal obturation as secondary prophylaxis for patients at high risk for recurrent variceal bleeding. Consecutive patients with HCC and/or PVT, or patients with non-HCC malignancy with PVT who had gastroesophageal variceal bleeding within 12 weeks were recruited. EUS-guided CYA injection was performed within 12 weeks of the index variceal bleeding for secondary prophylaxis. Oesophagogastroduodenoscopy (OGD) was performed before EUS to assess for presence of active bleeding or stigmata of recent bleeding from oesophageal varices (OV) and gastric vaices (GV). EUS was subsequently performed with a linear echoendoscope. OV and GV were assessed by B-mode imaging and Doppler on EUS for size measurement and vascular flow. Varices ≥ 3 mm were treated. CYA (0.5 ml of Histoacryl + 0.7 ml of lipiodol per injection) was injected with a 19 G needle under EUS guidance. Doppler was used to confirm variceal obliteration. Chest and abdominal x-rays were obtained to confirm satisfactory position of CYA/lipiodol. Patients were followed for 6 months after EUS or till death if patients died within 6 months of EUS. Follow-up EUS would be performed on day 90 and day 180 during which CYA injection may be repeated for recurrent varices. Outcome measures include cumulative incidence of rebleeding at day 30 and day 90, and complications related to the procedures. Death occurring prior to recurrent bleeding was considered a competing risk event in analysis.
**Results:** 23 patients were initially screened, with 20 patients meeting inclusion criteria and undergone EUS guided CYA injection (mean age 64+/-10; 85.0% male) successfully. 17 patients had HCC + cirrhosis, in which 88.2% also had PVT. Among these patients, the Barcelona Clinic Liver Cancer (BCLC) stage for the HCC were: A (5.9%), B (5.9%), C (88.2%), D (0%), and the Child-Pugh class were: A (41.1%), B (58.8%). The other 3 patients had non-HCC malignancy (gastric cancer, pancreatic neuroendocrine tumour, lymphoma) + PVT. In this cohort, 14 patients had OV bleeding and 6 patients had GV bleeding in the index bleeding episode before recruitment. In the 1st EUS, CYA injection was done for OV, GV, and OV + GV in 12, 6, 2 patients, respectively. 6 had varices ≥ 5 mm on EUS, while 14 had varices < 5 mm on EUS. The mean number of CYA injections performed in EUS was 1.4+/-1. The death adjusted cumulative incidence of rebleeding at 30-day and 90-day after EUS guided CYA injection were 15% (95% CI, 4 – 34) and 20% (95% CI, 6 – 40), respectively. 1 patient had mild dysphagia after CYA injection, but no serious adverse event occurred. Death occurred during the follow-up period were due to malignancy progression, organ failure or infection. 12 patients (60%) were alive and returned for 2nd EUS follow up at day 90 and 3 of the 12 patients (25%) needed additional CYA injection for treatment of recurrent OV or GV.
**Conclusion:** In this pilot study, EUS-guided CYA injection for variceal obturation as secondary prophylaxis for patients at high risk for recurrent variceal bleeding is safe and achieves a lower rate of recurrent variceal rebleeding when compared to previously reported data in the literature.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1305 ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE BY HEPATICOGASTROSTOMY FOR MALIGNANT HILAR BILIARY OBSTRUCTION IS A HELPFUL FEASIBLE PALLIATIVE TREATMENT IN DAILY PRACTICE

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**Introduction:** Malignant hilar obstruction is a common cause of endoscopic retrograde cholangiopancreatography (ERCP) failure or non feasibility for patients with surgical altered anatomy. Percutaneous transhepatic biliary drainage (PTBD) has poor results in re-intervention rate and quality of life.
**Aims & Methods:** A monocentric prospective study had been conducted in a tertiary-care-referral center (Cochin Hospital, Paris, France) including patients with modified surgical anatomy or after ERCP failure. Primary outcomes were technical and clinical success defined by decrease of 50% of total serum bilirubin level at 7 and 30 days. Secondary outcomes were procedure-related complications, administration rate of chemotherapy, hospital length stay, reintervention rate and overall survival rates.
**Results:** 18 patients had hepaticogastrostomy and 27.7% of them had transhilar stenting. Cause of obstruction were: local recurrence of primitive malignancy (33.3%), primitive pancreatic mass (22%), Klastkin tumor (16.7%) and carcinosis (16.7%). 61.1% of patients presented surgical modified anatomy and 30.8% presented proximal duct obstruction after ERCP failure. Technical success was achieved in 94% of patients, early clinical success in 72.2% of patients and late clinical success in 68.8% of patients. Procedure-related complication rate was 16.7%, chemotherapy administration rate was 55.6%, hospital length stay was 16 (7–45) days, reintervention rate at three months was 16.7% and mean overall survival rate was 79 (5–345) days.
**Conclusion:** EUS-HGS is a feasible technique for hilar obstruction after ERCP failure or for patients with surgical altered anatomy. Moreover EUS-HGS is a helpful technique in chemotherapy administration for patients with advanced disease
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1306 PROSPECTIVE STUDY FOR COMPARISON OF ENDOSCOPIC ULTRASOUND-GUIDED TISSUE ACQUISITION USING 25- AND 22-GAUGE CORE BIOPSY NEEDLES IN SOLID PANCREATIC MASSES

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**Introduction:** Although thicker needles theoretically allow more tissue to be collected, their decreased flexibility can cause mechanical damage to the endoscope, technical failure, and sample blood contamination. The effects of needle gauge on diagnostic outcomes of endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) of pancreatic mass lesions remain unknown.
**Aims & Methods:** This study compared procurement rates of histologic cores obtained from EUS-FNB of pancreatic masses using 25- and 22-gauge core biopsy needles. From March 2014 to July 2014, 66 patients with solid pancreatic mass underwent EUS-FNB with both 25- and 22-gauge core biopsy needles. Among them, 10 patients were excluded and thus 56 patients were eligible for the analyses. Needle sequences were randomly assigned, and two passes were made with each needle, consisting of 10 uniform to-and-fro movements on each pass with 10 mL syringe suction. A pathologist blinded to needle sequence evaluated specimens for the presence of histologic core.
**Results:** The mean patient age was $65.8 \pm 9.5$ years (range, 44–89 years); 35 patients (62.5%) were men. The mean pancreatic mass size was $35.3 \pm 17.1$ mm (range 14–122.3 mm). Twenty-eight patients (50%) had tumors at the pancreas head or uncinate process. There were no significant differences in procurement rates of histologic cores between 25-gauge (49/56, 87.5%) and 22-gauge (46/56, 82.1%, $P = 0.581$) needles or diagnostic accuracy using only histologic cores (98% and 95%). There were no technical failures or procedure-related adverse events.
**Conclusion:** The 25-gauge core biopsy needle could offer acceptable and comparable outcomes regarding diagnostic performance including histologic core procurement rates compared to the 22-gauge core biopsy needle, although the differences were not statistically significant.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1307 A RANDOMIZED CONTROLLED TRIAL COMPARING EARLY DEPLOYMENT OF A VIDEO CAPSULE VERSUS CONVENTIONAL WORK-UP OF NON-HEMATEMESIS GASTROINTESTINAL BLEEDING: INTERIM ANALYSES

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**Introduction:** Gastrointestinal bleeding (GIB) is a common diagnosis in the emergency department (ED). For hematemesis, the diagnostic algorithm is non-controversial. For non-hematemesis GIB (NHGIB), the algorithm is less clear, since the bleeding can originate anywhere in the gastrointestinal (GI) tract. For NHGIB, clinicians use signs and symptoms to assess where the most likely source of bleeding is and then choose the most appropriate endoscopic procedure. If, during this workup, a clinician is able to localize active bleeding or the likely source of bleeding (SOB) this may permit therapeutic intervention and reduce readmission rates for rebleeding. Our hypothesis is that early deployment of a video capsule (VCE) in patients presenting with NHGIB will shorten time to diagnosis, improve diagnostic yields, and improve visualization of SOB compared to the current standard of care.
**Aims & Methods:** Study inclusion criteria are > 18 years old, admission to the hospital, hemodynamic stability, no contraindications to VCE, and presentation with new onset NHGIB. If eligible they are consented and randomized into either the early capsule group (EC) or the standard of care group (SC).
Patients in the EC group swallowed an EC-10 Olympus VCE immediately following consent. The EC-10 real time viewer (RTV) was used to confirm entry into the stomach and to look for gastric bleeding. After completion images were processed, reviewed, and the further procedures were performed based on the findings. The SC group received care and procedures at the direction of the GI attending.
**Results:** A total of 150 patients were screened and 42 were enrolled. Baseline characteristics of the study patients are described in Table 1. The EC group had a significantly higher rate for detecting active bleeding or stigmata of recent bleeding (73.9% vs. 15.8%; $p < 0.001$) and rate of diagnosis (78.3% vs. 36.8%; $p = .006$) compared to the SC group. There was no significant difference between the EC and SC group in the rate of therapeutic intervention (30.4% vs. 15.8%; $p = 0.267$), total number of invasive procedures performed (1.0 vs. 1.1; $p = 0.463$), and length of stay (103 hours vs. 99 hours; $p = 0.913$). Kaplan-Meier curves analyzing time to diagnosis in both groups were significantly different (log-rank test, $p = 0.01$). Subgroup analysis of patients in the study found to have SOB demonstrated that a significantly larger percentage of those patients had a therapeutic procedure (45% vs. 4.5%, $p = 0.002$) and significantly less likely to have recurrence of bleeding in 30 days (0% vs. 19%, $p = 0.04$) compared to patients not found to have SOB. Elevated admission BUN, decreased admission systolic blood pressure, elevated Glasgow-Blatchford score, and receiving an early capsule were all significantly associated with finding SOB. Using these factors, a multivariate logistic regression was performed demonstrating that early capsule endoscopy was the only significant factor for predicting the presence of SOB (OR 94.3, 95% CI 4.6–1917.6).

**Table 1:** Descriptive statistics of patients based on cohort.

| n | Early Capsule 23 | Standard of Care 19 |
|---|---|---|
| Age (years), mean (SD) | 66.5 (10.9) | 74.1 (12.9) |
| Male, n (%) | 11 (47.8) | 12 (63.2) |
| Prothrombin time at admission (seconds), mean (SD) | 14.6 (6.2) | 22.8 (16.6) |
| Blood urea nitrogen at admission (mg/dL), mean (SD) | 30.6 (22.9) | 29.1 (20.7) |
| Hemoglobin at admission (g/dL), mean (SD) | 9.6 (3.0) | 9.3 (1.9) |
| Medication use prior to study, n (%) | | |
| Antiplatelet agent | 6 (26.1) | 10 (52.6) |
| Anticoagulation agent | 5 (21.7) | 8 (42.1) |
| NSAID agent | 4 (17.4) | 3 (15.8) |
| Reason for admission, n (%) | | |
| Guiac positive stool with anemia | 3 (13.0) | 0 (0.0) |
| Hematochezia with anemia | 6 (26.1) | 4 (21.1) |
| Melena | 13 (56.5) | 14 (73.4) |
| Unexplained anemia | 1 (4.3) | 1 (5.3) |
| Systolic blood pressure (mm Hg) at admission, mean (SD) | 119.6 (18.6) | 130.2 (17.8) |
| Heart rate (beats per minute) at admission, mean (SD) | 74.5 (10.2) | 77.1 (11.1) |
| Recent syncope, n (%) | 3 (13.0) | 0 (0.0) |
| Glasgow-Blatchford Score, mean (SD) | 8.4 (4.6) | 8.7 (3.7) |

**Conclusion:** Our study demonstrates that the early capsule has significant benefits compared to standard of care with regards to diagnostic efficiency and

locating signs of bleeding. In order to continue to evaluate additional outcomes more patients need to be studied and a multi-centered trial should be considered.
**Disclosure of Interest:** K. Bhattacharya: Dr. Bhattacharya serves as a consultant for Olympus Medical Systems.
D. Cave: Dr. Cave serves as a consultant for Capsovision, Medtronics, and Olympus Medical Systems.
All other authors have declared no conflicts of interest.

## P1308 VALIDATION OF SPICE, A METHOD OF DIFFERENTIATING SMALL BOWEL SUBMUCOSAL LESIONS FROM INNOCENT BULGES ON CAPSULE ENDOSCOPY

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**Introduction:** Small bowel submucosal lesions (SBSL) and innocent bulges, smooth protrusions of normal mucosa resulting from loop angulation and/or the impression of an adjacent loop, may have an identical appearance and can be difficult to distinguish on small bowel capsule endoscopy (SBCE), mainly if we exclude protrusions with alarm signs. Recently, Girelli et al proposed a score, smooth, protruding lesion index on capsule endoscopy – SPICE, in order to differentiate both.[1]
**Aims & Methods:** We aimed to evaluate and validate SPICE as a differentiation method between innocent bulges and SBSLs. We evaluated all SBCEs performed in our department between January 2005 and September 2015, and selected the ones with a smooth, round, protruding lesion in the small bowel. Lesions with alarm signs were excluded. A video clip of the region of interest was created and SPICE was assigned blindly and independently by two endoscopists. We evaluated demographic and clinical data and determined the discriminative ability of SPICE, using the definitive diagnosis of each patient as the standard criteria.
**Results:** We included 30 SBCEs of 28 patients (mean age $54.5 \pm 18.3$ years; 53.6% male), corresponding to 12 SBSLs (4 gastrointestinal stromal tumors, 2 neuroendocrine tumors, 4 lipomas and 2 polypoid lymphangiectasias) and 18 innocent bulges. SPICE scores ranged from 0 to 4, allowing the distinction between SBSLs and innocent bulges ($p < 0.001$). SPICE $> 2$ had 66.7% sensitivity, 100.0% specificity, 100.0% positive predictive value and 78.3% negative predictive value and the area under the curve was 0.88 (95% CI, 0.73–1.00; $p < 0.001$) for the diagnosis of SBSL.
**Conclusion:** Our data support SPICE, namely a score $> 2$, as a predictive method of SBSLs. Taking into account its simplicity, it may be very useful in the distinction between SBSLs and innocent bulges at SBCE.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1309 DEVELOPMENT OF A COMPUTED CLEANSING SCORE TO ASSESS THE QUALITY OF BOWEL PREPARATION IN COLON CAPSULE ENDOSCOPY

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**Introduction:** Colon capsule endoscopy (CCE) does not possess an objective and reliable scoring system to assess the quality of visualization of the colon mucosa. A previously published study (1) showed a computed assessment of small bowel mucosal visibility based on the ratio of color intensities of the red and green channel of the tissue color bar to be feasible and reproducible.
**Aims & Methods:** The aim of this study was to establish and validate a colonic Computed Assessment of Cleansing (C-CAC) score, based on the intensity of diverse ratios of color intensities of CCE still frames, to discriminate the 'adequately cleansed' from the 'inadequately cleansed' ones, with the highest performance. Twelve CCEs, using the Pillcam® Colon 2 system (Medtronic), were prospectively selected amongst a database, irrespective of the indication. All exams had allowed visualization of the entire length of the colon. All exams were considered normal. Subsequently, a C-CAC score, defined as the ratio of color intensities such as red over green (R/G ratio), and red over brown (a mixture of red and green, $R/(R+G)$ ratio) was calculated for each of the 79496 extracted colonic frames. Eighteen and sixteen intervals of a variable width (0.05 and 0.01, for each type of ratio, respectively) were then determined, ranging from the smallest to the largest ratio amongst the extracted frames. Then, twelve frames were randomly selected in each of these intervals, for both types of ratio. Two sets of 216 and 192 still frames were thus obtained (for R/G and $R/(R+G)$, respectively). These images were shuffled, and analyzed twice in a random order, by two experienced CCE readers, blinded to the C-CAC scores. A qualitative evaluation was performed based on criteria in the setting of small bowel CE (2): each image with a visualization of over 90% of the mucosa, with no, minimal or mild fluid and debris, bubbles, and bile/chyme staining, and with no, minimal or mild reduction of brightness, was considered to be 'adequately cleansed'. Any image failing to fulfill these criteria was considered as 'inadequately cleansed'. Images were subsequently classified as being 'adequately' or 'inadequately' cleansed (according to an experts' agreement when necessary). A receiver operating characteristic (ROC) curve was forged for both types of ratios. Thus, a C-CAC score threshold was established, yielding the highest diagnostic performance in terms of adequate cleansing assessment.
**Results:** In the first dataset (R/G ratio), 37 frames (17.1%) were 'adequately cleansed', the remaining 158 being 'inadequately cleansed' (82.9%). According to the ROC curve, a C-CAC score threshold of 1.55 was most performant to discriminate adequately from inadequately cleansed frames, with a sensitivity of 86.5%, a specificity of 77.7%, a positive predictive value of 44.4%, and a negative predictive value of 96.5%. In the second dataset ($R/(R+G)$ ratio), 22 frames (11.5%) were 'adequately cleansed', the remaining 170 being 'inadequately cleansed' (88.5%). According to the ROC curve, a C-CAC score threshold of 0.58 was most performant to discriminate adequately from inadequately cleansed frames, with a sensitivity of 95.5%%, a specificity of 62.9%, a positive predictive value of 25.0%, and a negative predictive value of 99.1%.
**Conclusion:** The two proposed C-CAC score based on the ratio of color intensities (R/G and $R/(R+G)$ ratios) come with high sensitivities and negative predictive values to discriminate 'adequately cleansed' from 'inadequately cleansed' CCE still frames, but they lack specificity. Further refinement, with implementation of additional image parameters, will overcome this limitation. These findings set path to future studies assessing the proportion of 'adequately cleansed' frames of CCEs, allowing to compare different colon-cleansing regimens in a objectve manner.
**Disclosure of Interest:** X. Dray: I have received lecture fees from Given Imaging / Covidien / Medtronic
All other authors have declared no conflicts of interest.

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## P1310 THERAPEUTIC IMPACT OF COLON CAPSULE AS A PAN-ENTEROSCOPIC TEST

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**Introduction:** Colon capsule is a non-invasive device primarily designed for colonic visualization. However, a slight modification of the ingestion protocol may allow both the visualization of the small bowel and colon with only one prep and one capsule. This pan-enteroscopic study might be useful for those patients who may have pathology in the small and large intestine (for instance in Peutz Jeghers syndrome) but also for those patients with gastrointestinal bleeding who are high-risk patients for anesthesia or for endoscopy.
**Aims & Methods:** We have included all pan-enteroscopic capsule procedures performed in our unit, from October 2011 to January 2015. We have retrospectively reviewed the clinical history, reason for referral and capsule findings. Creatinine and electrolytes pre and post procedure have also been gathered. All patients underwent the same colon prep, with PEG in split dose (2 liters + 2 liters) and sodium phosphate as capsule booster (30 ml + 15 ml).
**Results:** 68 patients were included (64.7% male). The mean age was 67 years old (21–90) and 45.6% were inpatients. The reason for referral was occult-obscure gastrointestinal bleeding (OGIB) in 14.9% of cases, overt-OGIB in 16.2%, 38.8% were high-risk patients for anesthesia/endoscopy (53.7% because of cardiac conditions) and had iron deficiency anemia, in 4.5% a Peutz Jeghers syndrome was suspected and 25.6% of patients underwent pan-enteroscopic for other reasons (diarrhea, abdominal pain...) The most frequent small bowel findings were angiodysplasia (23.5%), erosions/ulcers (13.2%) and polyps (8.8%). The most frequent colonic findings were diverticula (46.8%), polyps (50%), angiodysplasia (27.4%) and colon cancer (3.2%). In 38% of cases, the pan-enteroscopic capsule had a therapeutic impact, mainly referring the patient to balloon enteroscopy, colonoscopy or surgery. Despite of having several cardiac patients and even patients with renal insufficiency, no abnormalities were detected in post prep creatinine and electrolytes. We had one complication, as the capsule was retained in a small bowel bleeding stricture that was not suspected. This patient needed surgery to remove the stricture and the retained capsule.
**Conclusion:** The election of performing a pan-enteroscopic capsule had a therapeutic impact in almost 40% of cases. The pan-enteroscopic capsule is a relatively safe procedure, with no effect on renal function despite the use of sodium phosphate in high-risk patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1311 DEVELOPMENT AND VALIDATION OF A HIGHLY SENSITIVE AND HIGHLY SPECIFIC COMPUTED ASSESSMENT OF CLEANSING SCORE FOR SMALL BOWEL CAPSULE ENDOSCOPY

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**Introduction:** An objective and reliable scoring system is much needed to assess the quality of visualization in small bowel (SB) capsule endoscopy (CE), for both clinical practice and research purposes. A previously published study showed a computed assessment of SB mucosal visibility based on the ratio of color intensities of the red and green channels of the tissue color bar to be feasible and reproducible (1).

**Aims & Methods:** Thirty-three SB-CE were selected amongst a database of cases of obscure gastro-intestinal bleeding. The SB2 Pillcam® system (Medtronic) had been used. All exams had allowed full visualization of the small bowel. All were considered normal. For every SB-CE, the red, green and blue (R, G, B) components were extracted from each still frames of these videos. Subsequently, the SB-CAC score, defined as the ratio between the red and green pixels (R/G ratio), was calculated for each of the 443,141 extracted frames. Twenty-four intervals of R/G values of a 0.05 width were then determined, ranging from the smallest to the largest R/G ratio amongst the extracted frames. Then, twelve frames were randomly selected in each of these intervals. A first set of 288 still frames was thus obtained. These images were shuffled twice into a random order, and analyzed twice by two experienced SB-CE readers, blinded to the SB-CAC score of each image. A qualitative evaluation was performed based on the criteria previously used by Brotz et al. (2): each image with a visualization of over 90% of the SB mucosa, with no, minimal or mild fluid and debris, bubbles, and bile/chyme staining, and with no, minimal or mild reduction of brightness, was considered to be 'adequately cleansed'. Any image failing to fulfill these criteria was considered as 'inadequately cleansed'. Images were thereby analyzed as being 'adequately' or 'inadequately' cleansed (3 or 4 concurrent assessments out of 4 reads). In cases of discrepancy after initial analysis, an agreement was reached between the two readers and the image was subsequently classified. Once an 'adequately cleansed' or 'inadequately cleansed' qualification was allotted to every still frame (each of which with a previously calculated R/G ratio), a receiver operating characteristic (ROC) curve was forged. Thus, a SB-CAC score (R/G ratio) threshold was established, yielding the highest diagnostic performances in terms of adequate cleansing assessment. A second dataset of 288 different SB still frames was then generated, as described above, and read twice in a random order by two other experienced SB-CE readers, using the same blinded methodology. The diagnostic performances of the SB-CAC score threshold were then calculated, allowing validation of this score.

**Results:** In the first dataset, 130 frames (45.1%) were analyzed as being 'adequately cleansed'. According to the ROC curve, a SB-CAC score threshold of 1.6 achieved best to discriminate adequately from inadequately cleansed frames, with a sensitivity of 91%, a specificity of 91%, a positive predictive value of 89.4%, and a negative predictive value of 92.9%. In the second dataset, 114 frames (41.0%) were analyzed as being 'adequately cleansed'. The SB-CAC score threshold value of 1.6 was validated using this second dataset, yielding the following performances: sensitivity 93.6%, specificity 88.0%, positive predictive value 83.6%, and negative predictive value 95.5%.

**Conclusion:** The SB-CAC score based on the R/G pixels ratio has a threshold value of 1.6 with the highest sensitivity and specificity to discriminate 'adequately' from 'inadequately' cleansed SB-CE still frames. This constitutes an objective, reproducible, reliable, automated and comprehensive cleansing score for SB-CE. These findings set path to future studies assessing the proportion of 'adequately cleansed' frames of SB-CEs, allowing to compare different bowel-cleansing regimens. A similar CAC score in the setting of colonic CE is currently being generated. Further research is warranted in order to determine which proportion of 'adequately cleansed' frames defines an acceptable overall SB-CE quality in clinical practice.

**Disclosure of Interest:** X. Dray: I have received lecture fees from Given Imaging / Covidien / Medtronics
All other authors have declared no conflicts of interest.

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## P1312 CLINICAL UTILITY OF THE PATENCY CAPSULE

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**Introduction:** In patients with suspected or known obstructive gastrointestinal pathology, the use of patency capsule (PC) aims to minimize the risk of subsequent retention of the endoscopic capsule. However, its clinical utility is not consensual.

**Aims & Methods:** Our aim was to evaluation of the indications, results and safety profile of the PC. We performed a retrospective analysis of PCs (Agile patency Capsule) conducted between 2011 and 2015. Patency evaluation was performed after 30 hours, with radiological confirmation if PC was detected.

**Results:** We included 369 PCs, 54% female. The average age was $42 \pm 16$ years. Main indications included suspected Crohn's disease (CD) (45%), CD staging (32%), neoplastic diseases (9%), radic enteritis (3%), prior surgery (3%), NSAIDs enteropathy (2%) and anemia (2%). Before the exam 5% of patients were taking constipation-induced medications and 5% reported occlusive symptoms. 38% of patients had previous abdominal surgeries, most often ileal resection due to CD (24%). 42% of patients had previous imaging studies, revealing strictures in 20% and bowel dilation in 11%. Patency capsule was negative (patent gastrointestinal tract) in 73% of cases at 30 h and 2% of PCs were fully recovered in the following days. Seven patients (2.5%) showed self-limiting occlusive symptoms during the procedure. All patients with negative PC subsequently performed capsule endoscopy with no cases of retention. History of occlusive symptoms ($p = 0.023$) and strictures in imaging studies ($p = 0.029$) were associated with the detection of the PC at 30 hours.

**Conclusion:** PC is a safe and effective exam. Occlusive symptoms and imaging strictures were significantly associated with the retention. The retention rate was 25%, a similar result to that described in other series but higher than expected for the various indications, suggesting the importance of new research studies.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1313 SMALL BOWEL MALIGNANCY IN PATIENTS UNDERGOING CAPSULE ENDOSCOPY IN A TERTIARY CARE ACADEMIC INSTITUTION

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**Introduction:** Cancer of the small-bowel (SB) is rare, accounting for < 5% of all gastrointestinal (GI) neoplasms [1].Furthermore, diagnosis of SB cancer is often delayed [2]. Capsule endoscopy (CE) has become the procedure of choice for non-invasive diagnosis of SB diseases [3]. Nevertheless, data on the use of CE in diagnosis of SB cancer is limited [4].

**Aims & Methods:** Retrospective study; the records of all patients who underwent SBCE at our centre from Mar 2005 – Oct 2015 were reviewed; we retrieved those whose CEs were reported as suggestive of neoplasia. Further data was gathered on preceding and subsequent investigations, management and outcomes of these patients.

**Results:** From a total of 1949 CE studies (1082 PillCam™/867 MiroCam™), SB neoplasia was diagnosed in 8 patients (0.41%; 2 F/6 M; median age 56, range 34–72). Two had lymphoma, 3 gastrointestinal stromal tumours (GIST), 2 duodenal adenocarcinomas, 1 jejunal metastasis from a sarcomatoid lung tumour. In these patients, CE was performed for: iron-deficiency anaemia (IDA) ($n = 6$), diarrhoea ($n = 1$) & suspicion of SB lymphoma ($n = 1$). 7/8 patients had priornegative bidirectional GI endoscopies; 1 had a normal gastroscopy. Prior to CE, two patients had abdominal USS, 4 had CT scan, 2 had SB follow-through and 1 had a bone marrow aspirate. Two patients had capsule retention; one was removed with a gastroscope, the other with push enteroscopy. All 8 patients had further investigations after CE. Six had a chest, abdomen & pelvis CT scan for staging. Two patients had push enteroscopy, both of whom were diagnosed with duodenal adenocarcinoma. One had double balloon enteroscopy (DBE), two had colonoscopy, two had UGIE; there was one abdominal USS and one bone marrow aspirate. Four patients underwent SB resection. Following resection, 1 patient with GIST had imatinib chemotherapy. Of the two individuals with duodenal adenocarcinoma, one underwent gastroenterostomy and the other had an elective Whipple procedure. Four patients passed away. Two remain under follow up with oncology and two with the GI team.

**Conclusion:** SB cancers are rare and our experience is in agreement with other studies. The median age of 56 indicates that SB malignancy is more common in relatively younger patients. Unexplained iron deficiency anaemia was the main presenting complaint in our patients which triggered further investigation despite negative bidirectional endoscopies. CE is effective in picking up SB neoplasia where other imaging modalities have failed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1314 A COMPARATIVE STUDY OF FOUR MATERIALS FOR THE DEVELOPMENT OF NOVEL DUODENAL-JEJUNAL BYPASS LINER

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**Introduction:** The paradigm in the treatment of obesity and metabolic disease is changing from surgical therapies to minimally invasive endoscopic procedures. Therefore, endoscopic treatment such as duodenal-jejunal bypass liner has emerged as alternative therapies to bariatric surgery or medical therapy for weight loss. Although various materials (silicon, fluoroethylene, propylene, etc.) would be available for medical device, the optimal material for duodenal-jejunal bypass liner was not fully investigated. In this study, we compared the physical properties and characteristics of the materials for the duodenal-jejunal bypass liner.
**Aims & Methods:** Four test membranes were made of hydrophobic silicone, thin e-PTFE (Poly-tetra-fluoroethylene), thick e-PTFE, and FEP (Fluorinated ethylene-propylene). We performed the test for anti-tensile ability, durability, and the experimental aging test in pH2 and pH7 buffer solutions. The features of test materials were shown by using scanning electron microscopy (SEM) and infrared spectroscopy (FT-IR).
**Results:** The debris and cracks in surface on hydrophobic silicone were significantly increased after accelerated aging test with pH 2, 7 by SEM image. And it showed about 50% reduction in tensile force after the test. Thin-PTFE and thick e-PTFE showed the small amounts of debris on the surface after accelerating test by SEM. FEP had minimal changes on surface morphology after accelerating test. Anti-tensile ability of e-PTFE (thin and thick) was 10 times more than silicone, and 5 times than FEP in pH7 environment. The difference of anti-tensile ability between e-PTFE and FEP decreased in pH2 environment. There was no significant difference of anti-tensile between thin and thick e-PTFE. In the experimental aging test, FEP had better aging resistance and superior chemical stability than e-PTFE under corrosion environment. FEP showed a minimal FT-IR curve change on graph presenting a chemical property.
**Conclusion:** FEP and e-PTFE showed acceptable results in tensile force test and chemical resistance test. Whereas FEP material had a good chemical stability, both thin and thick e-PTFE had a superior tensile strength. Because of its poor anti-tensile force and durability, hydrophobic silicone material would not be appropriate for duodenal-jejunal bypass liner. It would be recommendable materials both FEP and e-PTFE for making the liner of new endoscopic duodenal-jejunal bypass stent.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1315 EUS-GUIDED ENTERO-ANASTOMOSIS WITH LUMEN APPOSING METAL STENT: PRELIMINARY ASSESSMENT OF INDICATIONS, EFFECTIVENESS AND SAFETY

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**Introduction:** Endoscopic Entero-Anastomosis (EEA) is a novel procedure performed in animal models and exceptionally in patients, without a case series published to date.
**Aims & Methods:** We want to present a retrospective study of 16 patients in whom EEA has been done in our center, describing the type of anastomosis performed, complications encountered and the results obtained. We identified retrospectively from a prospective database from 01/01/12 to 30/06/15, 16 patients with a mean age of 71.1 years (SD 11) underwent EEA. A prosthesis Axios® 15x10 mm was used in all patients, and its were placed under Echoendoscopy control. Sedation was performed with Propofol. One patient was excluded from the analysis due to lack of window.
**Results:** In 10 patients with post-surgical anatomy it was performed to access the bile duct: via gastro-jejunostomy (40%), jejuno-jejunostomy (40%) and percutaneous jejunostomy (20%). We obtained technical success in 80%, and clinical success (defined as the possibility of access to the bile duct) in 60%, with 20% of complications (jejunal tear, perforation) and stent migration due to the passage of the duodenoscope through the stent. In 5 patients, all oncologics, EEA was performed because of gastric outlet obstruction, with failure of conventional endoscopic treatments. 80% by gastro-jejunostomy, the remaining 20% by gastro-duodenostomy. Technical success in 60%, clinical success in 40% (clinical success was defined as the ability of the patient to tolerate an oral diet). The complication rate was 20% (1 patient) with perforation, peritonitis and subsequent death. There was no migration of the stent during trans-stent procedure with a pediatric or convencional endoscope.
**Conclusion:** EEA seems a safe procedure to facilitate biliary access in patients with postsurgical anatomy and to solve the gastric outlet obstruction in cases of malignant obstruction in patients with null surgical possibilities.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1316 SURVEILLANCE IN ESOPHAGEAL ATRESIA PATIENTS: ENDOSCOPY SHOULD BE A ROUTINE IN POST OPERATIVE?

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**Introduction:** Esophageal strictures remain the most frequent complication after surgical repair of esophageal atresia (EA) and occurs in 18% to 50% of patients. It is controversial whether the endoscopy is performed routinely after EA repair or only in symptomatic patients.
**Aims & Methods:** The aim of this study was to assess the frequency of esophageal stenosis in EA patients operated in a pediatric hospital in Rio de Janeiro, Brazil. A retrospective longitudinal study was carried out on patients with EA who were submitted to surgical repair in a period of 5 years in a pediatric hospital in Rio de Janeiro, Brazil. The data collected were age, sex, type of EA, associated congenital anomalies, type of surgery performed, evaluation of esophageal stenosis and recanalization of the tracheoesophageal fistula, time between first endoscopy and surgery and treatment performed for complications. The characteristic of these patients were collected from charts, operative and endoscopy reports. Symptoms suggestive of stenosis included dysphagia, vomiting, cough, poor or slow feeding, foreign body obstruction, recurrent respiratory tract infections, and/or poor weight gain. All patients presenting symptoms underwent digestive endoscopy. When stenosis was diagnosed, anastomotic dilatation were carried out.
**Results:** Forty-one patients were included in this study, and twenty-four were male (58.5%). Thirty-six children (87.8%) had EA with distal fistula and 5 (12.2%) EA with proximal fistula. Thirty-four patients (82.9%) were submitted to surgical repair with ligation of the fistula and 7 were submitted to gastric transposition after esophagostomy and gastrostomy. The surgery was performed on average nine days after birth. Eighteen (43.9%) children had congenital anomalies associated.
Twenty-one patients (51.2%) underwent digestive endoscopy, the first endoscopy was perfomed on average 11 months after surgery. Fourteen patients (34.1%) had stenosis of anastomotic and were submitted to esophageal dilatation. Four (9.8%) had recanalization of the tracheoesophageal fistula and were referred to surgery.
**Conclusion:** Esophageal stricture occurred in nearly one-third of patients in this series. Recanalization of the tracheoesophageal fistula is rare, but requires early treatment to avoid complications. Sometimes the symptoms are non-specific and the infant may develop serious complications before diagnosis. In our study, endoscopy was performed on average 11 months after surgery in symptomatic patients. Endoscopy performed by an experienced professional has a low index of complications, and although further studies are needed to follow up these patients, we recommend early routine endoscopy in all infants after EA repair to detect complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1317 RADIOACTIVE STENT FOR ESOPHAGUS CARCINOMA

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**Introduction:** Radioactive stents have shown improvement in survival for patients with terminal esophageal cancer (1). However, loading brachytherapy seeds into current brachytherapy stent designs is a manually intensive process that can result in direct seed-esophagus contact, dose hotspots and mucosal ulceration or perforation.

**Aims & Methods:** Our aim is to develop an improved radioactive stent design that can achieve, using a porcine preclinical model, a conventionally acceptable dose of 60 Gy to the esophageal tumor while preserving the health and structural integrity of the surrounding esophagus and peri-esophageal normal tissues. Monte Carlo calculations of radiation transport simulations (MCNP6) were performed to optimize the stent design in terms of dose uniformity and surface hotspots. Using standard endoscopy techniques, 20 mm diameter stents were implanted in 3 minipigs (31–39 kg) with a radiation dose target of 60 Gy at a 5 mm mucosal/submuscosal depth. Over the 60 day implant the pigs were regularly monitored, including endoscopy and radiography. After 60 days, the stents were removed and the pigs were sacrificed at 1, 2, and 3 months following stent removal to assess short-term side effects. A full gross necropsy and histopathological analysis was performed on each pig.
**Results:** Monte Carlo simulations showed that increasing the number of seeds, using a polymeric stent instead of a metal stent, and placing the seeds inside the stent wall improved dose uniformity at the prescription distance, while reducing hotspots at the mucosa. The stent was constructed with 6 interior channels designed to accept 6 strands with 10 seeds each for a total of 60 seeds per stent (model 6720 I-125 Seeds-in-Carrier, GE Healthcare).The I-125 source strength (0.5 U/seed) was determined for a 2-month implant. This design also allowed for fast and safe loading of the radioactive seeds. During stent assembly, extremity exposure was less than 2 mSv. Whole body exposure was much less given use of Pb gowns and a transparent L-block shield. Each stent was safely loaded with the radioactive seeds, deployed in the esophagus within 1 cm from the intended location, and sutured to the esophagus through a neck incision to prevent stent migration. The maximum radiation exposure rate at 1 meter from each implanted pig was less than 0.004 mSv/h, thus not introducing concerns for radiation safety during pig monitoring over the course of the study. Follow up from this study will be completed by the time of the meeting, and late-breaking results on histopathological results will be reported.
**Conclusion:** A novel stent design was combined with stranded brachytherapy seeds to produce a radioactive stent for eventual treatment of esophageal cancer in humans. Initial results of this preclinical study suggest that the stent design is capable of delivering the desired target dose to an esophageal tumor.
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## P1318 ENDOSCOPIC TREATMENT OF POST-LAPAROSCOPIC SLEEVE GASTRECTOMY LEAKS WITH A SPECIFICALLY DESIGNED METAL STENT

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**Introduction:** Laparoscopic Sleeve Gastrectomy (LSG) is one of the most used restrictive surgical procedures for the treatment of morbid obesity. Leak of the surgical suture at the level of the esophago-gastric junction is the main complication of LSG; endoscopic therapy of such a complication has been achieved using clips, fibrin glue, bioprosthetic plug, plastic and metal stents (1, 2). The role of non-specifically designed Self-Expandable Metal Stent (SEMS) in the treatment of post-LSG leaks is not well established and reported results are not satisfactory (stent migration, ulcer impaction, stent incarcerations) (1). The efficacy of a specifically designed fully covered SEMS (FC-SEMS) as a first-line therapy in post-LSG leaks, is evaluated.
**Aims & Methods:** Patients referred to our Endoscopy Unit from January 2013 to November 2015 for the treatment of post-LSG fistula underwent insertion of a specifically designed FC-SEMS (Niti-S Beta stent, Taewoong Medical, Seoul, Korea). This stent has a small cell meshes, a specific design with anti-migration features (outer double layers coated with silicone) and a length between 18 and 23 cm to extend from the esophagus to the antrum, in order to bypass the leak; stent diameter is 24 mm (32 mm proximal flared end) to have an optimal adherence to the esophagus.
**Results:** Ten patients (5 males, mean age 32.1 years, range 20–53) (mean BMI 43.11, range 31–66) with a post-LSG leak were treated. Characteristics and results for each patient are shown in **Table 1**. A total of 11 SEMS were inserted. In 2 patients a bioprosthetic plug (Surgisis, Cook Inc.) was also placed. In 8 patients (80%) the fistula healed after stent removal. Two patients (20%) had fistula recurrence after 8 and 14 days from stent insertion; these 2 cases were treated with a FC-SEMS with wide cells meshes. In one case proximal dysfunction of the stent was diagnosed, the stent was removed and replaced with the same FC-SEMS but with small meshes design, obtaining subsequent fistula healing. The second patient had also proximal stent dysfunction leading to the development of an infected 4 cm collection; 2 double-pigtails plastic stents (diameter 8.5 French, length 2 cm) were inserted from the leak to the collection obtaining an internal drainage; fistula healing was observed after plastic stents removal. In 2 patients (20%) gastric ulcerations secondary to impaction of the distal end of the stent were observed at stent removal; it was an incidental finding without any adverse event. After a mean follow-up of 13 months (range 5–37) all the patients are asymptomatic.
**Conclusion:** A specifically designed esophago-gastric FC-SEMS with a small cells design, is an effective and promising treatment for post-LSG leaks, but needs further evaluation in large series and in the setting of clinical trials.
**Disclosure of Interest:** A. Tringali: Boston Scientific Corporation No current consulting agreements in place One day animal lab in 2012 and 2013. Speaking and teaching in 2014
I. Boskoski: Cook Inc. Consultant
G. Costamagna: Olympus Japan Grant/Research Support Cook, Inc Advisory Committees or Review Panels. Grant/Research Support Boston Scientific Corporation Advisory Committees or Review Panels. Taewoong Medical Inc Advisory Committees or Review Panels.
All other authors have declared no conflicts of interest.

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**P1318 Table 1:** Patients characteristics

| Patient n | Sex | Age | BMI | Time between LSG and SEMS placement (days) | Leak size (cm) | APC debride of leak margins | Bioprosthetic plug | SEMS length (cm) | Time between procedure and SEMS removal (days) | SEMS dysfunction | In hospital days after stent placement | Follow-up after SEMS removal (months) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 22 | 40.9 | 15 | < 1 | No | No | 23 | 43 | No | 11 | 37 |
| 2 | M | 20 | 42.8 | 68 | ≥ 1 | Yes | Yes | 20 | 49 | No | 5 | 24 |
| 3 | F | 27 | 42 | 54 | ≥ 1 | No | No | 20 | 46 | No | 4 | 19 |
| 4 | M | 20 | 40.5 | 120 | ≥ 1 | Yes | Yes | 20 | 37 | No | 4 | 16 |
| 5 | M | 23 | 49.4 | 27 | < 1 | No | No | 20 | 66 | No | 3 | 10 |
| 6 | F | 51 | 42.5 | 27 | ≥ 1 | No | No | 18 | 33 | No | 1 | 8 |
| 7 | M | 24 | 66.6 | 13 | < 1 | No | No | 20 | 36 | No | 2 | 5 |
| 8 | F | 53 | 40.2 | 16 | ≥ 1 | No | No | 20 | 32 | No | 1 | 5 |
| 9 | F | 39 | 31 | 141 | < 1 | No | No | 20 | 14 | Yes | 2 | 5 |
| 10 | M | 42 | 35.2 | 28 | < 1 | No | No | 20 | 8 | Yes | 1 | 5 |

APC = Argon Plasma Coagulation SEMS = Self Expandable Metal Stent LSG = Laparoscopic Sleeve Gastrectomy

## P1319 ULTRA-LONG BENIGN ESOPHAGEAL STRICTURES HAVE POOR OUTCOME

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**Introduction:** Strictures of ≥2 cm length are also termed complex esophageal strictures. In contrast to non-complex short esophageal strictures, only few information is available on the outcome of long (≥2 cm) and ultra-long esophageal strictures (≥5 cm). In the context of emerging esophageal endoscopic techniques (EMR, ESD, RFA) we expect that post-procedure strictures as well as post radiation will account for the majority of long and ultra-long esophageal strictures in the future. Their treatment is currently not evidence based, however relies on expert opinion from small case series.
**Aims & Methods:** We aimed to investigate the outcome of long (≥2 cm) benign, intrinsic esophageal strictures. 83 consecutive patients were identified who underwent endoscopic treatment of benign, intrinsic esophageal strictures of ≥2 cm length at a single tertiary between 7/2010 and 5/2014. Strictures and dilations of these patients prior to this time interval where evaluated based on retrospective review of outside hospital records and patient recollection. Data collected from the time interval 7/2010 and 5/2014 was abstracted also by retrospective chart review, including stricture etiology, duration of presence of stricture, endoscopic procedures and long-term outcome. The main endpoints were to calculate the treatment success defined as improved dysphagia score and resolution of dysphagia, as well as the rate of gastrostomy-dependent patients and patients requiring esophagectomy.
**Results:** 83 patients (mean age 63 years, SD 16.9; 54% female) were followed over 17 months (mean) at our facility for esophageal strictures of 53 months (mean) duration. Stricture etiology included peptic 23%, radiation 26%, anastomotic 11%, post-ablation 11%, post-EMR 10%, dermatologic conditions 10% and others 9% strictures, with a mean length of 43 mm [range 20–200] and mean diameter of 8.4 mm [range 1–11]. Median dysphagia score at presentation to our facility was 2 (able to swallow semi-solid only). Patients underwent a median of 7 dilations, which correspondents with 0.3 dilations per months. Only a minority of patients underwent in addition to dilation argon plasma tissue vaporization, stent placement, steroid and Mitomycin-C application. Median dysphagia score remained unchanged at 2, with 14% of patients having resolution of dysphagia, whereas 61% patients experienced unchanged or worsened dysphagia. 25% were eventually gastrostomy-dependent and 4% required esophagectomy. Stricture length and diameter remained not significantly changed at end of follow up. Kaplan-Meier analysis delineated resolution of dysphagia according to stricture length: 50% in strictures 20–49 mm, 12.5% in 50–99 mm and 0% in ≥100 mm. Limitations: Single center, retrospective study, heterogeneous cohort.
**Conclusion:** Endoscopic treatment is effective in only 50% for long (≥2–5 cm) esophageal strictures as reflected by improvement of dysphagia score. However, dysphagia remained unchanged in most ultra-long strictures (≥5 cm). Gastrostomy or esophagectomy were long-term required in 29% of strictures ≥2 cm.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1320 OUTCOMES OF SELF-EXPANDABLE METAL STENTS IN THE PALLIATIVE TREATMENT OF GASTRODUODENAL OBSTRUCTION: A SINGLE-CENTRE EXPERIENCE

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**Introduction:** Malignant gastric outlet obstruction (MGOO) affects patients with advanced gastric, duodenal, periampullary and pancreatic cancers and causes significant morbidity with resultant impairment of quality of life[1]. This condition may be resolved with palliative interventional procedures, either endoscopic or surgical; surgical procedures are associated with a prolonged hospital stay and sometimes with poor function of the gastroenterostomy[2]. Endoscopic placement of a self-expandable metallic stent is an option in these patients. It is well-tolerated and associated with shorter hospital stay, low complication rate and a rapid symptom relief, allowing the intake of food in these patients[2]. This efficacy can be measured by the gastric outlet obstruction (GOOS) score.
**Aims & Methods:** We performed a retrospective single-center study including consecutive patients with malignant gastric outlet obstruction who underwent an uncovered metallic stent placement in our Department from January 2012 to December 2015. We collected data from patients' records. Our primary outcomes were technical and clinical success (this one measured by GOOS score); secondary outcomes were duration of stent patency and survival. Statistical analysis was executed on SPSS® version 20.0.
**Results:** Twenty-seven patients were included: 17 (62.3%) were men, with an age of 69 ± 10 years (44–99 years). The type of tumor was: gastric adenocarcinoma (14 patients - 52%), pancreatic adenocarcinoma (10 patients – 37%) and cholangiocarcinoma (3 patients – 11%). The location of the obstruction was: pylorus (14 patients - 52%), the bulb (5 patients – 19%) or the other duodenum portions (8 patients – 29%). The technical success rate of the procedure was 100%. The clinical success rate was achieved in 23 patients (85%), with 18 patients with a GOOS > 1 (able to eat solid or semi-solid food). Patients restarted oral intake 35.5 hours after stent placement (24–168 hours). The median hospital stay was 17 ± 10 days. There weren't complications related to the procedure. Stent restenosis occurred in 5 patients (19%) during the follow-up period and was resolved with the placement of a second stent. The mean survival of the patients was 58 days.
**Conclusion:** Metallic stent placement is an effective and relatively safe procedure in the palliative treatment of patients with MGOO allowing a better quality of life. Our primary outcomes results' are in accordance to recently published results, which report a technical success of 95–100% and a clinical success of 90–95%[2–3].
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1321 FEATURES OF ESOPHAGEAL STENTING USING ULTRATHIN ENDOSCOPE

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**Introduction:** Self-expanding metallic stents (SEMS) is a well-established form of palliative treatment for dysphagia in esophageal cancer. Different methods of esophageal stenting have its own features, advantages and limitations. Ultrathin endoscopes (UTE) guided SEMS placement is simple and time-saving technique [1]. It is safe, effective, and not requires fluoroscopic assistance.
**Aims & Methods:** The aim of this study was to assess the features and safety of UTE-guidance technique stent placement under direct vision, and compare it with standard stenting techniques using X-rays. The study included 182 patients (143 M/39F, mean age 72) who were undergoing stent placement for malignant esophageal strictures, between July 2010 and April 2016. 58 patients (32%) had cardioesophageal cancer, 106 (58%) – tumor in the distal part of esophagus and 18 (10%) - in the proximal part of esophagus. All patients were incurable. Stent was placed by a standard procedure using direct visual control with standard endoscope and fluoroscopy in 40 patients (group A). 142 patients were undergone by UTE-guided SEMS placement without fluoroscopy (group B). We used ultrathin endoscope with a diameter of 4.7 mm (GIF N180, Olympus Comp.). Partially SEMSs from 80 mm to 140 mm in length was used.
**Results:** In all cases the technical success rate was 100%. In group A, in 7 cases (17.5%) the length of the stent was selected incorrectly. We could not pass the endoscope through the "waist" of stent immediately after expansion and to assess the distal flanges of the stent in most cases. We had to re-reposition of stent in 3 cases (7.5%). The technical success rate of UTE-guided SEMS placement (group B) was in all cases. It allowed us to avoid intraoperative complications and significantly simplified the technical stent placement procedure. The use of ultrathin endoscope allows accurately assess the length of malignant stenosis, even tortuous esophagus lumen [2,3,4]. UTE-guided SEMS placement does not require fluoroscopy to demarcate the proximal and distal extent of the lesion. In all patients, the proximal and distal stent positions could be seen and corrected at once. The mean time required for SEMS placement was 25 minutes in group A, and 15 minutes in group B.
**Conclusion:** The standard procedure for SEMS insertion requires fluoroscopic guidance for accurate stent deployment and adjustment of positioning during the procedure. SEMS placement using ultrathin endoscopes might have some advantages over with standard method. UTE-guided SEMS placement without fluoroscopy improves the conditions for precise positioning of stent; It allows to select stents individually with minimal risk of complications for the patient; It allows to control the stent installation process, which affects the technical success of stenting.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1322 USE OF TEMPORARY SELF-EXPANDABLE METALLIC STENT PLACEMENT IN POST-GASTRECTOMY COMPLICATION

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**Introduction:** The self-expandable metallic stent (SEMS) in upper gastrointestinal (GI) tract has been used for palliative treatment of malignant conditions. Recently, the use of SEMS is expanded to the benign esophageal or gastroduodenal strictures. Also its temporary use in patients with postoperative complication, such as anastomosis site leak or stricture, was reported. However, there are scarce data available regarding efficacy, long-term complications and outcomes with use of SEMS in benign disease, especially postoperative complications.

**Aims & Methods:** We retrospectively analyzed 39 patients who underwent a self-expandable metallic stent insertion in upper GI tract for postoperative complications between March 2009 and December 2015. All patients underwent curative gastrectomy for gastric cancer. Data collected included patient demographics, indication for procedure, type of stent used, complications, and patient outcomes.

**Results:** SEMS placement was technically successful in all patinets. At 2.5 years mean follow-up, no severe adverse events were observed after the procedures. Of 39 patients, 21 patients (53.8%) had SEMS placed for anastomosis site leakage, 8 (20.5%) for anastomosis site stricture, 10 (25.6%) for luminal narrowing due to angulation, such as E loop or A loop syndrome. After SEMS placement, symptomatic improvement was achieved in 37 of 39 patients (94.9%), while no improvement was noted in 2 patients (5.1%). Among 37 patients with symptomatic improvement, 2 patients (5.4%) had recurrent symptom and underwent repeated stent insertion and balloon dilatation respectively. After SEMS placement, mean timing of initiating diet was 7.2 days, and mean duration of hospitalization was 17.1 days. Migration was only reported complication, and developed in 9 (23.1%) patients. SEMS endoscopic removal or spontaneous expulsion was failed in 5 patients (12.8%); 1 pateint underwent sugery for SEMS removal due to migration, 1 patient failed due to stent overgrowth, and 3 were remained SEMS in place due to patient's will.

**Conclusion:** SEMS placement is effective and safe treatment for post-gastrectomy anastomosis site leaks, stricture and obstruction due to E loop or A loop syndrome. It can lead to decrease burden and risk of re-operation related mortalities and modalities.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1323 ENDOSCOPIC MANAGEMENT OF COMPLICATIONS OF SELF-EXPANDABLE METAL STENTS FOR TREATMENT OF MALIGNANT ESOPHAGEAL STENOSIS AND TRACHEOESOPHAGEAL FISTULA

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**Introduction:** Self-expandable metal stent (SEMS) implantation may rapidly improve the symptoms of malignant esophageal stenosis and tracheoesophageal fistulas (TEF). However, dysphagia often returns subsequently and repeated endoscopic intervention may be necessary.

**Aims & Methods:** We analyzed retrospectively the clinical data of 212 patients with locally advanced esophageal cancer who underwent SEMS implantation. The risk factors of complications, frequency and efficacy of repeated endoscopic interventions were examined.

**Results:** 238 SEMS implantations were performed with 99.06% technical success and 0.01% procedure related deaths rate in the enrolled 212 cases. Complications occurred in 84 patients (39.62%) and in 55 cases (25.94%) repeated endoscopic procedures were required. Early re-intervention 24–48 hours after the stent implantations was necessary due to stent migration (12 cases), arrhythmia (2 cases), intolerable retrosternal pain (1 case) and dyspnea (1 case). An average of 1.98 (range 1–6; median: 2) repeated gastroscopies 13.58 (range 1.5–48; median: 11) weeks after the stent implantation were performed during the follow-up period: 37 stent repositions, 23 re-stent implantations, 15 endoscopic esophageal dilations and 7 stent removals. In 48 cases (87.3%) oral feeding of patients made possible by endoscopic interventions.

**Conclusion:** In one quarter of SEMS implantations the occurrence of complications, that can successfully manage by endoscopic interventions, has to be reckoned with. Our experiences have shown that the individualized stent choice may substantially reduce the complications rate and make repeated endoscopic interventions easier.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1324 PREDICTORS OF COMPLICATIONS AND MORTALITY IN SELF-EXPANDING METAL STENTS FOR PALLIATION OF MALIGNANT COLONIC OBSTRUCTION

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**Introduction:** Self-expanding metal stents (SEMS) for palliative purposes in malignant colonic obstruction is an alternative to surgery, that has gained popularity over times, since surgery is associated with high mortality and morbidity, as well as detrimental impacts on a patient's quality of life.

**Aims & Methods:** Retrospective study of patients submitted to SEMS for palliation of obstructing malignant colorectal cancer from 2005 to 2015. Chi-square test and Student's t-test were used to compare non-continuous and continuous data, respectively. Survival and progression-free survival were calculated using Kaplan-Meier method and Log-Rank test. Multivariate analysis using Cox proportional hazard models was used to evaluate the predictors of survival and complications.

**Results:** 45 patients were included with high rates of technical and clinical success (97.7% and 95.5% respectively), with complications occurring in 18% of the patients (8.8% perforations, 4.4% obstruction and 4.4% migration). The length of the stenosis was superior in the patients with complications (74.3 vs 54.7 mm, $p = 0.02$) but the local of the stenosis was not associated with complications. 11.1% of the patients had a re-intervention (2.2% surgery and 8.8% colocation of other SEMS). The median duration of the hospitalization was 5 days after SEMS. The mortality rate was 37.2% at 30 days, 56.5% at 60 days and 87.5% at 1 year. There were no identified predictors of survival, including age, sex, stage of the tumor, metastasis or complications of the procedure.

**Conclusion:** In this study, SEMS placement was associated with high rate of technical and clinical success, with low rate of complications, giving an option for palliate patients with obstructive neoplasia. The length of the stenosis was associated with a greater risk of complications and although the majority of SEMS procedures were performed in rectosigmoide colon, the right colon obstruction was also managed endoscopically without increasing number of complications.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1325 ENDOSCOPIC GASTRODUODENAL SELF-EXPANDABLE METAL STENT PLACEMENT: REVIEW OF OUTCOME IN A LARGE ACUTE UK HOSPITAL

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**Introduction:** Gastroduodenal obstruction is commonly a late sign of locally advanced or metastatic cancer with a poor prognosis (mean survival 100 days[1]) and a poor associated quality of life[1]. Current treatment strategies include the placement of self-expandable metal stents, a palliative gastrojejunostomy or placement of a venting percutaneous gastrostomy tube. Placement of gastroduodenal self-expandable metal stents has emerged as the leading treatment option for gastroduodenal obstruction.

**Aims & Methods:** The aim of the study was to review the outcome of endoscopic SEMS placement for malignant gastroduodenal obstruction in a large acute UK hospital. All patients who underwent gastroduodenal self-expandable metal stents placement between January 2009 and October 2015 were identified using the hospital endoscopy reporting system (HICSS). The electronic records for these patients were reviewed, recording the underlying pathology, sedation used, time between procedure and death and all complications occurring within 30 days that were a cause of death.

**Results:** A total of 115 gastroduodenal self-expandable metal stents were placed in 103 patients (35 uncovered and 80 partially covered). Stent dysfunction occurred in 11.7% of cases with 11 patients undergoing repeat procedures due to tumour overgrowth (4), stent fracture (3), stent displacement (2), and failure of stent to expand (2). One patient underwent two repeat procedures due to tumour overgrowth. 60 cases were performed under general anaesthetic and the remainder (55) under conscious sedation. The underlying pathology included pancreatic adenocarcinoma (37), gastric adenocarcinoma (17), duodenal adenocarcinoma (5) cholangiocarcinoma (4), ampullary cancer (3) and carcinoid tumours (3). The remainder of cases were metastatic disease (18) or unknown (16). Median survival following gastroduodenal self-expandable metal stents placement was 53 days (range 2–805 days). Three patients died within 30 days of self-expandable metal stents placement; two from pneumonia and one from perforation of the caecum unrelated to the stent. The remaining patients died as a result of the underlying primary malignancy.

**Conclusion:** Endoscopic gastroduodenal self-expandable metal stents placement appears a feasible and effective treatment option for patients with malignant gastroduodenal obstruction. Stent dysfunction and complications rates, and median survival in our series were similar to previously published data[2]. Further data on quality of life following gastroduodenal self-expandable metal stents insertion and cost-effectiveness are required.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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WEDNESDAY, OCTOBER 19, 2016 09:00–17:00

**SURGERY III – POSTER EXHIBITION**

## P1326 WHAT IS THE EXPERIENCE OF UK GENERAL SURGERY TRAINEES IN RELATION TO HAEMORRHOIDECTOMY: OPERATIVE NUMBERS, PROCEDURE-BASED ASSESSMENTS AND THE ASSOCIATION BETWEEN THESE?


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**Introduction:** Current guidance for UK Certificate of Completion of Training (CCT) in general surgery from the Joint Committee on Surgical Training (JCST)[1] recommends trainees with a colorectal interest to have performed 15 haemorrhoidectomies and to have achieved three procedure-based assessments (PBAs) rated at level four. We aimed to determine the experience of current UK surgical trainees in performing haemorrhoidectomy and the relationship between operative numbers and PBA levels achieved.

**Aims & Methods:** We used data from the Intercollegiate Surgical Curriculum Programme (ISCP) database[2] linked to the eLogbook[3] for all UK trainees from August 2007 to October 2014. Trainees awarded CCT during the period studied and those still in training were included. We identified all trainees undertaking a haemorrhoidectomy PBA and operative records for all trainees for haemorrhoidectomy.

**Results:** In total we identified 1431 trainees. Trainees performed 23182 haemorrhoidectomies with 65% (n = 15160) either under supervision or performed. Some 585 trainees recorded a total of 1289 PBAs for haemorrhoidectomy with a median of 2 (inter quartile range (iqr) 1–3, range 1–15) per trainee. PBA performance was graded as level four in 42% (543), level three in 38% (493), level two in 20% (252) and one as level one. Over 88% (66/75) of trainees recording three level four PBAs had performed more than 15 haemorrhoidectomies. The median number of procedures performed prior to achieving three level four PBAs was 33 (iqr 21–44).

**Conclusion:** Current indicative operative numbers for haemorrhoidectomy do not reflect the number of procedures that are reported prior to obtaining three level four PBAs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1327 NOMOGRAM PREDICTS STOMA REVERSAL RATE AFTER LOW ANTERIOR RESECTION WITH COVERING ILEOSTOMY


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**Introduction:** Although a temporary ileostomy is widely used in protecting the anastomosis after middle and low rectal cancer surgery, some of the patients do not fully achieve stoma closure after primary surgery.

**Aims & Methods:** Thus, the aim of this study was to identify risk factors for permanent stomas following low anterior resection or inter-sphincteric resection with a temporary ileostomy for rectal cancer and to develop a nomogram that can predict non-reversal ileostomy within a year. To develop a nomogram, we reviewed retrospectively the clinical data of 212 consecutive rectal cancer patients who underwent low anterior resection or inter-sphincteric resection with or without a temporary stoma between April 2012 and June 2015 at the University of Tokyo Hospital. The predictive accuracy and discriminative ability of the nomogram were determined using concordance index (C-index) and a calibration curve. Statistical evaluations were done using the multivariate analysis and Cox hazard model.

**Results:** Among 212 patients with rectal cancer, 116 had a temporary ileostomy, 11 had a temporary colostomy, and 85 were without stoma creation. Among temporary ileostomy cases, 90 (77.6%) patients showed stoma reversal, the median period for which was 6.9 months from the time primary resection surgery was performed for rectal cancer. The temporary and permanent stoma groups consisted of 87 and 29 patients, respectively. The nomogram included the depth of invasion (p = 0.037), other metastatic organs (p = 0.017), and preoperative chemo-radiotherapy (p = 0.086), which were based on the multivariate analysis and results obtained from the Cox hazard model. The calibration curve showed good concordance between the predicted and actual probabilities of one-year stoma non-reversal rates. The C-index of the nomogram was 0.635.

**Conclusion:** Permanent stoma risk for the rectal cancer patients, who had temporary stomas after low anterior resection or inter-sphincteric resection, was characterized by higher depth of invasion and metastasis in other organs. In this study, the nomograms could identify rectal cancer patients with a higher risk of long temporary ileostomy, helping surgeons in correctly choosing the type of stoma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1328 METASTATIC SMALL BOWEL ADENOCARCINOMA: SERIES OF 34 RESECTIONS


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**Introduction:** Small Bowel Adenocarcinoma (SBA) is a rare tumor and the therapeutic management is not well established. The curative treatment of resecable tumor and its metastases is carcinological surgery. Metastatic surgery has never been studied. SBA at a metastatic stage is usually treated with an exclusive palliative chemotherapy (CT) with overall survival (OS) between 8 and 22 months. The benefit of metastases resection has not been demonstrated. The aim of our study was to assess a medical-surgical strategy including carcinological surgery of metastases.

**Aims & Methods:** The study cohort included 34 patients with SBA at a metastatic stage with a carcinological resection of the primary tumor and metastase (s). Patients included in the study came from the NADEGE prospective cohort (n = 27) and additional patients were included through the AGEO network (n = 7) (French Association of Gastroenterologists and Oncologists). The primary endpoint was OS. Secondary endpoints were the assessment of progression-free survival (PFS) and survival prognostic factors in univariate analysis, and the description of metastases' localizations.

**Results:** Thirty-four patients were enrolled, including 25 with synchronous metastases and 9 metachronous. Patient characteristics were similar to those of the entire NADEGE cohort except for the localization of the primary tumor which was more frequently ileal (29.5% vs. 16%; p = 0.049) and less frequently duodenal (41% vs 59% p = 0.043). Metastases' localizations were peritoneal (n = 10), liver (n = 9), lymph node (n = 4), lung (n = 1), multiple (n = 5) and other (n = 5). For the metastatic carcinological resection, seven patients had invaded resection margins (R1 n = 4 and R2 n = 3) and 24 had healthy margins. The median OS was 25.1 months and PFS was 13.6 months. Four patients received neoadjuvant CT. CT adjuvant after resection of the metastases was performed on 29/34 (85%) of patients, mostly by FOLFOX (n = 25). In univariate analysis, factors associated with decreased OS were: poorly differentiated histology (15.1 vs 28.1 months p = 0.004), resection margins invaded at surgery in the metastatic stage (16.6 vs 27.6 p = 0.014) and lymph node involvement at surgery of the primary tumor (23.3 vs 43.2 p = 0.040). The best prognosis factor was adjuvant CT with oxaliplatin compared with adjuvant CT without oxaliplatin (29.5 vs 16 months p = 0.034).

**Conclusion:** SBA's surgery metastases was for the first time assessed with this study. Overall survival appeared greater compared with non-operated patients with metastatic SBA observed in the literature. Tumor differentiation, possibility of an R0 resection and existence of an initial nodal involvement should be considered for a better selection of surgical indications.

**Disclosure of Interest:** All authors have declared no conflicts of interest.


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## P1329 SURGICAL TREATMENT OF ENTEROVESICAL FISTULA – DOES SUTURING URINARY BLADDER MATTER?

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**Introduction:** Enterovesical fistula (EVF) is a rare chronic disease represented by an abnormal communication between the bladder and the intestine. Management of EVFs is mainly dependent on the underlying pathology, site of the bowel lesion, and patient's preoperative clinical status. The EVF's treatment involves the conservative approach and surgical procedures. The aim of the most frequently used operative method is to resect and reanastomose the offending bowel segment and to close the bladder. However, recent studies express debut whether the closure of defect in the urinary bladder wall is always needed. The aim of this study was to analyze the most appropriate surgical treatment approaches in patients with EVF. We would like to underline the problem of intraoperative suturing of the bladder defect.
**Aims & Methods:** Fifty-nine patients with EVF, who underwent surgical treatment, were enrolled. A surgical one-stage procedure with resection and anastomosis of the offending bowel segment in all enrolled patients was performed. After the separation of the offending bowel segment, the permeability of the bladder was checked by feeding a methylene blue through a catheter into the bladder lumen. In all patients a drainage of the bladder by a Foley catheter was made for seven days after the operation.
**Results:** The most common intestinal fistula involving urinary bladder was colovesical fistula observed in 52.5% cases. The most often observed primary disease related with the EVF involving colon was diverticulitis: 67.7% of patients. The statistical analysis showed no differences between EVF with urinary bladder sutures and without them in terms of all perioperative complications. During a median follow-up of 48 months (range 3 to 103) the recurrent episode of EVF formation in one patient with urinary bladder suturing and in two patients without suture were observed ($p = 0.913$); all in CD patients.
**Conclusion:** Nowadays surgery seems to be the treatment of choice in patients with EVF. Our study showed that the closure of bladder defect is not necessary in cases without intraoperative leakage of liquid delivered by catheter to bladder lumen.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1330 NEW SURGICAL APPROACH IN PREVENTION OF ANASTOMOTIC LEAKS IN PATIENTS WITH COLON OBSTRUCTION

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**Introduction:** Anastomotic leakage remains an urgent problem in colorectal surgery. In elective surgery on colorectal cancer, it is 10–17.9%, while complicated forms - 3–32%, mortality - 10–50% [1,2,3]. Surgeries on obstructive ileus in 26–85% are closed by overlapping colostomy. The majority of patients with stoma become socially and psychologically disadaptaited disabled. The second stage - reconstructive surgery is one of the most difficult operation in abdominal surgery with a high percentage of postoperative complications. The frequency restoration of physiologic passage through the colon can be perfomed only in 30–40% of patients.
**Aims & Methods:** Aim of study was to evaluate the safety, outcomes in patients with colon obstruction after resection with primary nonfunctional anastomosis (PNA) comparing with primary anastomosis. 155 patients with cancer of proximal rectum and sigmoid colon, complicated with acute ileus (included 12 patients with local peritonitis) were included and divided into 2 groups. In basic group ($n = 95$) PNA with preventive transversostoma (patent №72889) after resection of the rectum was performed. In comparing group ($n = 60$) resection of the colon with primary anastomosis was performed. We have worked out rate score of risk factors of anastomotic dehiscence. After resection proximal end of colon was sutured by stapler, through the colon was imposed two welt ligatures in cross direction which was lowered into the distal lumen. Traditional end-to-end anastomosis was supplemented. On 7–8 day welt ligatures were dragged out, afterwards necrosis of stitched stapler area of colon has been advanced, as result anastomosis has become passable. Stoma was closed in 2–2.5 month after operation.
**Results:** In the basic group, in 7 causes (7.4%) during the operation peritonitis were found (vs 5 cases (6,7%) in comparing group). 84 patients (88.4%) were radically operated (vs 57 patients (95%) in comparing group) and palliative operations were performed in 11 patients (11.4%) (vs 3 patients (5%) in comparing group). Combined operation with resection of posterior wall of the bladder, hysterectomy, small bowel resection was performed in 12 patients (12.6%) (vs. 16 patients (26.4%) in comparing group). General complications have arised in 5 (5.3%) of basic group and in 11 (18.4%) patients of comparing group. Anastomotic leakage have arised only in 1 (1.1%) patient of basic group and in 7 (11.7%) patients of comparing group. In all patients of comparing group with anastomotic leaks reconstructive operation wasn't performed. The average length of stay in hospital patients and control group was 15.2 and 16.0 days, to operations 2.2 and 3.2 days respectively.
**Conclusion:** PNA with preventive transversostoma provides adequate decompression of the colon, reliable prevention of colorectal anastomotic leakage, avoids complex reconstructive operations and is good alternative for Hartman's procedure. Application of primary nonfunctional anastomosis is not limited to colon obstruction, but is also appropriate to the presence of peritonitis. The anastomotic leakage appeared only in 1 patient (1.1%), indicating the high reliability of developed and applied in the primary nonfunctional anastomosis. Application of primary nonfunctional anastomosis is indicated if significant technical difficulties blending primary anastomosis in patients with multiple risk factors for anastomotic leak seams and anatomic features of the blood supply or the length of the mesentery or bowel segment proximal anastomosis, which may be risk of anastomotic leakage in the postoperative period.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1331 DISEASE FREE SURVIVAL IN THE YOUNG PATIENTS WITH COLORECTAL CANCER: A POSSIBLE ROLE FOR IMMUNESURVEILLANCE?

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**Introduction:** Colorectal cancer (CRC) is infrequent in patients under 50 years. According to recent studies [1], in this age group CRC could have more aggressive histopathological features but better survival outcome than older (over 50 years old) patients.
**Aims & Methods:** The aim of this study was to understand why younger patients with CRC have a better survival outcome in spite of worse clinical and pathological features. We retrospectively enrolled 26 patients under 50 years with CRC operated on in our Unit from January 2006 to December

2010. We matched them 1:2:2 with 52 patients from 50 to 70 years and with 52 patients over 70 years old. The matching was done according tumor site, stage and gender. Details about pre-operative parameters, laboratory data, surgical operation, histology and follow-up were retrieved. Non parametric statistics, ROC curve analysis and survival analysis were used.
**Results:** Patients under 50 years had a significantly longer overall survival ($p = 0.001$) and disease-free survival ($p = 0.05$) than older groups. However, they had more frequently lymphovascular invasion than the older groups ($p = 0.006$) and they more frequently developed metachronous CRC at follow up ($p = 0.03$). Nevertheless, preoperative lymphocytes blood count/white blood count ratio (LBC/WBC) inversely correlated with age at operation (rho = -0.21, $p = 0.04$) and it predicted CRC recurrence with an accuracy of 70%, $p < 0.001$ (threshold value LBC/WBC = 0.21%). Patients with a LBC/WBC ratio over this threshold had a significantly better overall and disease survival ($p < 0.0001$ and $p < 0.0001$, respectively). At multivariate analysis, stage and LBC/WBC ratio, but not age at operation, resulted independent predictors of disease free survival ($p = 0.0001$ and $p = 0.01$, respectively).
**Conclusion:** Patients under 50 years had a significantly longer overall survival and disease free survival than older groups. Overall survival is probably related to the presence of co-morbidities. On the contrary, better disease free survival, in spite of worse pathological features, of younger patients seems to be due to a higher LBC/WBC ratio. These results suggest a more efficiently functioning immune system and thus, a possible role of immunosurveillance in neoplastic control.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1332 FEASIBILITY AND SAFETY OF LAPAROSCOPIC AND ENDOSCOPIC COOPERATIVE SURGERY FOR GASTRIC SUBMUCOSAL TUMORS

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**Introduction:** Laparoscopic and endoscopic cooperative surgery (LECS) is a newly developed concept for the dissection of gastric submucosal tumors (gSMT), enabling preservation of the stomach or minimization of the extent of partial resection.
**Aims & Methods:** We aimed to evaluate the feasibility and safety of LECS.
The medical records of 27 patients with gSMT less than 5 cm in diameter who underwent LECS between June 2008 and January 2016 were retrospectively reviewed. Data evaluated included the demographic and clinical characteristics of patients and tumors; total procedure time and postoperative hospital stay; and success, complication, and recurrence rates.
**Results:** The 27 patients included 16 men and 11 women, aged 20–89 years (mean 62 years). These patients had 28 tumors, 23 in the upper third (U), three in the middle third (M) and two in the lower third (L) of the stomach. Median tumor size was 32.5 mm (range 13–55 mm). Of these 28 tumors, 21 were diagnosed postoperatively as gastrointestinal stromal tumors (GISTs), five as leiomyomas, and one each as a schwannoma and an aberrant pancreas. The R0 resection rate was 100%, with no patient requiring conversion to open surgery. The median total procedure time was 148 min (range 94–222 min), and the median postoperative hospital stay was 5 days (range 4–14 days). One patient (3%) experienced a complication, ileus. During a median follow-up period of 39 months (range 6–60 months), one patient (3%) experienced tumor recurrence, consisting of peritoneal dissemination.
**Conclusion:** LECS, which combines the advantages of both laparoscopy and endoscopy, completely resected all tumors without conversion to open surgery and achieved short postoperative hospital stay.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1333 LAPAROSCOPY ENDOSCOPY COOPERATIVE SURGERY (LECS) PROCEDURE TO BREAKTHROUGH THE LIMITATION OF ESD AND EMR FOR COLORECTAL TUMORS

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**Introduction:** We established the Laparoscopy Endoscopy Cooperative Surgery (LECS) procedure to overcome the limitation of colorectal ESD and EMR. We will report the usefulness of this epoch-making procedure from the viewpoint of safety and curability.
**Aims & Methods:** In this report, we will clarify the usefulness of LECS procedure applied with ESD technique to complete a safe one-piece resection with adequate surgical margin. We performed ESD on 1,229 colorectal tumors in 1,197 patients (male: female = 700:497; mean age, 65.9 years). Among these cases, 278 cases were accompanied by SM fibrosis. These cases were divided into three groups; absence of fibrosis (Type A), fibrosis due to benign causes (due to biopsy, recurrence after EMR, etc. Type B), and fibrosis due to cancer invasion in the SM layer (type C). The degree of fibrosis was classified into mild (grade 1), moderate (grade 2), and severe (grade 3) degree. In this study, we examined the limitation of ESD and established the indication of LECS procedure.
**Results:** The one-piece resection rates were as follows: Type A; 925/951(97.3%), Type B-1; 84/87(96.6%), B-2:46/52(88.5%), B-3:25/43 (58.1%), Type C-1:46/46(100%), C-2:19/20(95.0%), C-3:18/31(58.1%). We experienced four cases (0.3%) of perforation in Type B. In cases with Type B-3, one-piece resection becomes more difficult due to the risk of perforation. The limitation of ESD is thought to be existed in these lesions from the viewpoint of safety and curability. From these results, we established the LECS procedure applied with ESD technique to overcome the limitation of ESD. Indications of the LECS procedure for colorectal tumors were thought to be as follows; Intra-mucosal carcinoma and adenoma accompanied by wide and severe degree fibrosis due to tumor recurrence after endoscopic and surgical resection, submucosal tumors, tumors involved appendix or diverticle. We performed one-piece resection for 11 cases using LECS procedure, 3 case of mucosal cancer accompanied by severe degree fibrosis, and 2 cases of adenoma involved diverticle, 3 cases of mucosal cancer involved appendix, 2 case of submucoal tumor, and 1 case of poor endoscopic operability. We experienced no complications, and average hospital stay was 7.7(6 to 12) days.
**Conclusion:** We developed a LECS procedure to overcome the limitation of ESD and EMR, and completed one-piece resection of the tumors considered as high risk of perforation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1334 LAPAROSCOPIC NO-TOUCH PANCREATICODUODENECTOMY

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**Introduction:** One of the techniques, becoming more and more popular in open pancreatic surgery is no-touch pancreaticoduodenectomy (PD). Laparoscopic access could bring some advantages to pancreatic resections.
**Aims & Methods:** The aim was to determine possibility and safety of laparoscopic no-touch PD in patients with periampullary tumors. In the period 2013–2015 we performed 51 no-touch PD in our institute. Laparoscopic PD was completed in 6 patients, including 4 no-touch PD. Inclusion criteria at the learning stage were periampullary tumors without any potential contact to the main arterial and venous vessels, no signs of lymph node enlargement, no previous surgery on the upper level of the abdomen, no history of acute pancreatitis. The laparoscopic no-touch PD was completed in 4 patients. There were 2 male and 2 female patients aged from 36 to 63 years (mean age was 53 + 10 years). Tumors were localized in the ampulla of Vater in 1 patient, in pancreatic head- in 1 patient and in intrapancreatic portion of distal bile duct- in 2 patients.
**Results:** The mean duration of surgery was 443 ± 44 minutes (from 370 to 490 minutes). The mean blood loss was 650 ± 269 ml (from 300 to 1000 ml). In 3 patients (75.0%) postoperative complications were recorded in the form of pancreatic fistula grade B. Mortality was zero. In all patients R0 resection was achieved. One patient died 3 months after the surgery from the reasons neither connected to the surgery. 1 patient has been alive for 13 months being diagnosed a metastatic disease on the 9-th month. 2 patients are alive without signs of recurrence (20 months and 14 months).
**Conclusion:** No-touch technique could be done from laparoscopic access in a selected group of patients. Potential advantage is fast rehabilitation of patients with early start of adjuvant chemotherapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## WEDNESDAY, OCTOBER 19, 2016 09:00–14:00

## IBD III – POSTER EXHIBITION

### P1337 TWO NEW GENETIC MOUSE MODELS FOR ULCERATIVE COLITIS BASED ON LATERAL TIGHT JUNCTION DISRUPTION

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**Introduction:** A key pathogenetic feature of ulcerative colitis (UC) is an intrinsic low mucus phosphatidylcholine (PC) content. Recently a paracellular transport for PC across lateral tight junctions (TJ) has been described.

**Aims & Methods:** We aimed to prove the hypothesis that disruption of lateral TJ causes diminished luminal PC transport and induces an UC phenotype. We examined adult C57BL6 wildtype and mutated mice with tamoxifen inducible villin-Cre dependent intestinal deletion of kindlin 1 and 2 which were assumed to present with disrupted lateral TJ.
**Results:** Electron microscopy of mucosal biopsies of both mutants revealed loosening of lateral TJ with expansion of the mucosal crypt lumina. PC secretion into mucus was reduced by > 65% and the mucus PC content dropped from 80 in controls to 39 and 27 nmol mg mucin $2^{-1}$ in kindlin 1 and $2^{(-/-)}$ mice, respectively. In parallel the hydrophobicity was reduced from 72° in controls to 30° and 35° in kindlin 1 and $2^{(-/-)}$ mice, respectively. Accordingly microbiota penetrated into the submucosa. Later on, a full blown intestinal inflammation was present in both mutants with loose bloody stools as well as macroscopic and histologic features of colitis. The inflammation could be reversed by oral PC supplementation. In analogy, colonic biopsies of patients with UC also showed TJ disruption revealing widened crypt luminal diameters and functionally an impaired luminal PC secretion.
**Conclusion:** Genetic mouse models with intestinal deletion of kindlin 1 and 2 resulted in TJ disruption and revealed pathophysiologic features of impaired PC secretion to the mucus leading to mucosal inflammation compatible with human UC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1338 ROLE OF SLC26A3 (DRA) ION TRANSPORTER IN ENHANCING INTESTINAL EPITHELIAL BARRIER IN COLITIS

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**Introduction:** Slc26a3 ion transporter also known as DRA (downregulated in adenoma), is a $Cl^-/HCO_3^-$ exchanger, it absorbs $Cl^-$ and exports $HCO_3^-$ in a partly CAII-dependent fashion, and it contributes to intestinal fluid absorption and enterocyte acid/base balance. Recent research showed that loss of DRA impairs mucosal $HCO_3^-$ secretion and it may occur due to inflammation induced changes in the crypt and villous architecture or the effect of proinflammatory cytokines on epithelial ion transporters. And previous study indicated that Slc26a3 deficiency is associated with absence of a firm mucus layer and $HCO_3^-$/mucus barrier impairment in mice, thus $Slc26a3^{-/-}$ mice is susceptible to dextran sodium sulphate (DSS)-induced colitis. However, whether Slc26a3 had an effect on intestinal epithelial barrier is not clarified yet.
**Aims & Methods:** To elucidate its impact on epithelial barrier in colitis, we studied the role of DRA in epithelial barrier in acute dextran sulfate sodium (DSS) induced colitis in vivo and in Caco2BBE cells in vitro, then explored the potential mechanisms. The expression of DRA, TNF-$\alpha$ and tight junction (TJs) were detected in DSS-induced colitis mice by RT-qPCR, Western blot assay and Immunofluorescence staining. Then the colonic epithelial ultrastructure was investigated by transmission electron microscope. Next, after transfected DRA siRNA or lentiviral-mediated DRA overexpression in Caco2BBE cells, the expression of TNF-$\alpha$ and tight junction (TJ) proteins were measured by RT-qPCR and Western blot assay. The changes of TJs also measured when different dosage of TNF-$\alpha$ affect DRA overexpression Caco2BBE cells. Cell apoptosis was detected by FACscan flow cytometer (FACS) analysis.
**Results:** Transmission electron microscope results showed that tight junction was destroyed in distal colon of DSS treated mice. Compared to control group, mice treated with DSS showed a higher TNF-$\alpha$, much lower expression of DRA, Occludin, ZO-1 and Claudin1, inversely Claudin4 and Claudin5 were markedly increased. Knockdown of DRA in Caco2BBE cells reduced the expression of Occludin, ZO-1 and Claudin-1, and increased Claudin-5 expression, serum TNF-$\alpha$ level was also markedly elevated. On the contrary, overexpression of DRA resulted in the high expression of Occludin, ZO-1 and Claudin-1, decreased Claudin-5 expression and serum TNF-$\alpha$ level was significantly decreased. In addition, TNF-$\alpha$ could affect the expression of DRA and TJs in overexpression DRA Caco2BBE cells in dosage-dependent way. However, there's no significant difference between siDRA transfected and DRA overexpressed Caco2BBE cells in cell apoptotic rate.
**Conclusion:** These results suggest that DRA exhibit therapeutic potential against colitis and preserve intestinal epithelial barrier integrity through changing TJs expression which may be regulated by TNF-$\alpha$.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1339 CLINICAL CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE DIAGNOSED BEFORE OR AFTER OF PRIMARY SCLEROSING CHOLANGITIS (PSC): EFFECT ON PSC OUTCOME

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**Introduction:** Primary sclerosing cholangitis (PSC) is associated with inflammatory bowel disease (IBD) in 50–80% of cases, usually (80%) with ulcerative colits. Ulcerative colitis associated with PSC is characterised by backwash ileitis, rectal sparing, quiescent pancolitis and an increased risk of colorectal cancer compared to IBD without PSC (1). IBD-PSC has been regarded as a unique, distinct disease entity. However, many of the patients have had IBD long before the diagnosis of PSC (2). To this date, there are no data on clinical differences of IBD-PSC patients based on the preceding diagnosis. We evaluated the role of PSC as a disease modifier of IBD by studying the differences of PSC and IBD phenotypes based on the preceding diagnosis.
**Aims & Methods:** Patients were recruited from the PSC-registry of Helsinki University, consisting of 612 PSC patients. Inclusion criteria was met in 424 patients; the diagnosis of both diseases and a minimum follow-up time of 12 months. Patient recruitment was performed on tertiary care referral to ERCP procedure at primary PSC diagnosis or follow-up into registry. ERC findings were scored according to modified Amsterdam score [Helsinki score] (3). Routine colonoscopy was done for all patients at least at the time of PSC diagnosis.
**Results:** PSC preceded IBD in 20 (4.7%) patients, while PSC and IBD were simultaneously diagnosed in 84 (19.8%). Three-quarters of the patients had IBD preceding PSC and 75% of patients also had ulcerative colitis and nearly all of them presented with pancolitis (92.5%). The median age at time of diagnosis of IBD was 23 years in patients with diagnosis before PSC and 28 years in those diagnosed simultaneously or after. The median ERC score in patients with PSC preceding IBD was 6 (IQR 3–9) compared to 5 (IQR 2–8.25) in patients without PSC as preceding diagnosis ($p = 0.08$). Respectively, histological liver fibrosis stage 3 or 4 was observed in 6 (15.0%) and 10 (8.5%) patients ($p = 0.24$). Data on clinical characteristic are presented in Table 1.
**Conclusion:** Our study population is one of the largest on this topic. Our findings support previous studies on IBD often preceding PSC. PSC preceding IBD was associated with higher ERC score and more advanced liver fibrosis stage. Endoscopic and histologic IBD data are warranted to assess if PSC modifies the clinical course of IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1340 ENDOSCOPIC INJECTION OF MESENCHYMAL STROMAL CELLS INTO THE BOWEL WALL ATTENUATES EXPERIMENTAL COLITIS

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**Introduction:** Mesenchymal stromal cells (MSCs) are a new potential therapeutic modality in inflammatory bowel diseases because of their immunomodulatory properties and their participation in tissue repair processes. However, when injected intraperitoneally or intravenously only a small part of the cells, if any, reaches the inflamed colon. In previous experiments MSCs as spheroids administered intraluminally as enema into the colon were found to alleviate experimental colitis. In the present study we assessed whether endoscopically injected MSCs, as singe cells or in spheroids, into the intestinal wall of the inflamed distal colon also affect the course of experimental colitis.
**Aims & Methods:** A total of $2.0 \times 10^6$ green fluorescent protein (GFP)-positive single MSCs or 2000 GFP-positive MSC spheroids, formed from 1000 MSCs, were injected in every quadrant of the distal colon of C57BL/6 mice with established dextran sulphate sodium (DSS)-induced colitis ($n = 8$ per group). Body weight was measured daily and disease activity scored (i.e. loose stool, visible faecal blood and macroscopic inflammation) at time of sacrifice. Endoscopy was performed for injection of the MSCs and before sacrifice. The murine endoscopic index of colitis severity (MEICS) was used to evaluate mucosal damage. A subgroup of mice received luciferase transfected MSC

**P1339 Table 1:** Comparison of clinical characteristics and outcomes of PSC-IBD patients based on timing of IBD diagnosis.

| Variable | $N_{total}$ | Patients (n,%); median [IQR] | IBD preceding PSC (n = 320) | IBD diagnosed simultaneously (20) or following (84) PSC (n = 104) | p-value |
|---|---|---|---|---|---|
| Age, median [IQR] | 424 | 42 [33–54] | 43.5 [34–54] | 38.5[31–51] | $<0.05$ [a] |
| Gender, male | 424 | 274 (64.6) | 206 (64.6) | 68 (65.4) | 0.9 [b] |
| **IBD outcomes** | | | | | |
| IBD diagnosis age, years | 407 | 23 [18–32] | 22 [17–29] | 28 [22–37] | $<0.0001$ [a] |
| IBD duration at PSC diagnosis, years | 303 | - | 7 [3–14] | - | - |
| Ulcerative colitis | 422 | 316 (74.9) | 241 (72.8) | 75 (75.5) | 0.7 [b*] |
| *extent, pancolitis* | 248 | 248 (92.5) | 186 (92.1) | 62 (93.9) | 0.8 [b] |
| Crohn's disease | 91 | 91 (21.6) | 68 (21.3) | 23 (22.3) | - |
| *location, ileum* | | 11 (13.9) | 10 (12.6) | 1 (1.3) | 0.01 [b*] |
| *location, colon* | | 25 (31.6) | 13 (22.4) | 12 (57.1) | |
| *location, ileocolon* | | 43 (54.4) | 35 (60.3) | 8 (38.1) | |
| *behavior, luminal* | | 49 (71.0) | 29 (59.1) | 20 (100) | $<0.0001$ [b] |
| Intermediate colitis | 422 | 15 (3.6) | 10 (3.1) | 5 (4.8) | - |
| Colorectal carcinoma | 404 | 7 (1.7) | 6 (2.0) | 1 (1.0) | 0.7 [b] |
| Colectomy | 419 | 87 (20.8) | 75 (23.7) | 12 (11.7) | $<0.01$ [b] |
| **PSC outcomes** | | | | | |
| PSC diagnosis age, years | 423 | 31 [23–42] | 32 [24–43] | 28 [21–37] | $<0.01$ [a] |
| Intrahepatic PSC | 416 | 229 | 180 | 49 | 0.09 [b] |
| Intra- and extrahepatic PSC | 416 | 187 | 133 | 54 | |
| Liver histology: F3/4 | 158 | 16 (10.1) | 10 (8.5) | 6 (15.0) | 0.24 [b] |
| ERC-score | 397 | 5 [2–9] | 5 [2–8.25] | 6 [3–9] | 0.08 [a] |
| Biliary dysplasia or cholangiocarcinoma | 404 | 15 (3.7) | 12 (3.9) | 3 (3.0) | 1.0 [b] |
| Orthotopic liver transplant | 424 | 32 (7.5) | 23 (7.2) | 9 (8.7) | 0.67 [b] |

[a]Mann-Whitney U-test; [b]Fisher's exact test; [c]Chi-square test

spheroids to trace the spheroids ex vivo by bioluminescence (BLI). Paraffin embedded tissue was used for immunohistochemical localization of injected MSCs. Differences in expression profiles of relevant regulatory genes between MSCs grown in monolayer or in spheroids were assessed by quantitative PCR (qPCR) on mRNA isolated from MSCs and MSC spheroids in vitro.
**Results:** Endoscopically injected MSCs and MSC spheroids both alleviated DSS-induced distal colitis, as shown by a higher relative body weight (% body weight at the start) from day 3 up to day 6 after treatment compared to controls, with significant differences at day 5 (MSCs $88 \pm 3\%$ and MSC spheroids $87 \pm 2\%$ vs controls $79 \pm 2\%$, both $p < 0.05$). Furthermore, mice treated with single MSCs or MSC spheroids had a lower disease score compared to control mice (MSCs $1.8 \pm 0.3$, $p = 0.05$ and MSC spheroids $1.4 \pm 0.3$ vs controls $2.8 \pm 0.4$, $p = 0.01$), particularly due to less macroscopic inflammation. However, no differences in the MEICS were found. MSCs and MSC spheroids were found in the bowel wall by BLI and GFP staining 6 days after treatment. qPCR analysis showed transforming growth factor (TGF)-$\beta$1, TGF-$\beta$3, hepatocyte growth factor and C-X-C chemokine receptor type 4 to be upregulated whereas cyclo-oxygenase-2 and insulin-like growth factor-1, were downregulated in MSC spheroids compared to single MSCs.
**Conclusion:** Local injection of MSCs, into the inflamed distal colon as single cells as well as spheroids, is able to attenuate DSS-induced colitis and these MSCs remain in the bowel wall for at least 6 days after installation. Despite differential expression of several genes involved in immune regulation, tissue repair and trafficking, MSCs as single cells or spheroids give a similar efficacy. These data indicate the beneficial potential of local treatment with MSCs for distal colitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1341 A SCFA-RECEPTOR AGONIST SUPPLEMENTATION AS A NEW STRATEGY TO PROTECT AGAINST INTESTINAL INFLAMMATION IN MICE

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**Introduction:** Crohn's disease (CD) is a chronic and disabling inflammatory disorder of the intestine, and its prevalence and incidence are increased in developed countries. CD involves an interplay between intestinal microbiota, host genetics and environmental factors. Among factors associated with a Western lifestyle, changes in dietary habits and especially, the escalating consumption of fat and sugar parallels increased incidence of CD.
**Aims & Methods:** In this work, we aimed at better understanding the potential relationships between nutrition, gut microbiota composition and host's health by means of a suitable animal model. Thereby, we evaluated the potential protective effect of a G-protein-coupled receptor 43 (GPR43) agonist on gut inflammation following chemically-induced colitis or Adherent-Invasive E. coli (AIEC) infection in mice. Mice were fed a high-fat high-sugar (HF/HS) diet or a conventional diet for 18 weeks. E. coli populations associated with colonic and ileal mucosa were quantified using a culture-dependent method and confocal microscopy. Gut microbiota composition was analyzed by Illumina sequencing. Production of short-chain fatty acids (SCFAs) by microbiota was measured by gas chromatography in fecal samples of mice. GPR43 receptor was visualized by confocal microscopy after immunostaining of colonic mucosa tissues and in biopsies from CD patients. Mice treated or not with a GPR43 agonist were infected with AIEC bacteria or received DSS to induce colitis. Inflammatory parameters were measured to evaluate the effectiveness of GPR43 agonist treatment in the control of gut inflammation.
**Results:** Abnormal proportions of *E. coli* bacteria were recovered from colonic and ileal mucosa of mice under a HF/HS diet, compared to mice fed a conventional diet. Interestingly, intestinal mucosa dysbiosis was observed after Illumina sequencing characterized by a reduction of bacterial richness, but also an overgrowth of pro-inflammatory proteobacteria and a decrease in protective bacteria in mice fed a HF/HS diet. This was correlated with a significantly decrease of SCFAs concentrations. Moreover, GPR43 receptor expression was reduced in mice treated with a HF/HS diet and reduced in CD patients compared with controls. Mice treated with an agonist of GPR43 were protected against DSS-induced colitis and AIEC infection, showing a decrease of Disease Activity Index (DAI), lipocaline-2 level, cytokine release and mucosa-associated-AIEC bacteria.
**Conclusion:** Western diet creates an intestinal dysbiosis characterized by a decrease of protective SCFAs producing bacteria, favoring the overgrowth of opportunistic pathogenic *E. coli* which could aggravate the inflammatory process resulting in chronic inflammation. Moreover, regulation of GPR43 receptor expression could be used as a new strategy to treat patients abnormally colonized by AIEC bacteria.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1342 BIOLOGIC FUNCTIONS BETWEEN NON-AFFECTED AND AFFECTED MARGINS OF ILEUM SAMPLES FROM CROHN'S DISEASE PATIENTS WHO WILL DEVELOP POST-SURGICAL RECURRENCE

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**Introduction:** Transcriptome profile from ileocolectomy performed on non-affected margin of the ileum of the Crohn's disease (CD) patients showed changes in NOTCH signalling that could be implicated in early post-surgical recurrence (PSR). Comparing transcriptome profile from inflamed vs healthy margin could reveal new knowledge about the CD recurrence.
**Aims & Methods:** Objectives: To identify specific biologic functions between non-affected and affected margins of surgical samples from CD patients which will develop recurrence >18 months of the surgery. Material and methods: Transcriptomic profile study (CodeLink© microarrays, USA) among nonaffected and affected margins of ileocolestomy from CD patients with PSR (n = 5) or not PSR (n = 10) were performed. Ten controls were also included in this study and compared to different intestinal margins. Raw data from microarray analysis undergone quality control, normalization and clustering. Next analysis of gene differentiation was done with following statistical criteria: FDR < 0.05 or FDR < 0.01 and abs (log (FoldChange)) >2. The most relevant genes were grouped in co-expression modules using WCGNA (selection power=13, r2 > 0.92). GeneSet databases were used to perform enrichment analysis to screen biological and molecular functions in each module. The modules linked to recurrent or not recurrent CD were identified based on high correlation (abs (r2) > 0.75; p < 0.05).
**Results:** After quality control procedures a total of 53 samples and 20,902 gene expression probes mapping one gene were identified and included in further analysis. No single gene expression probe was identified when recurrent and no recurrent patients within the inflamed or non-affected margins were compared. However, 222 probes (69 with FDR < 0.01) were identified among non-affected and inflamed margins from CD recurrent patients, and 342 probes (95 with FDR < 0.01) showed different expression non-recurrent patients. These individual probes were grouped in 5 modules, three of them involved specifically in recurrent patients. Modules related to oxygen levels and protein amidation had a positive correlation between PSR and non-PSR (abs (r2) >0.96 and >0.83; p < 0.0003, respectively), while centriolecentriole cohesion showed a negative correlation (abs (r2) = -1; p = 10–9).
**Conclusion:** PSR in CD show highlighted biological functions related to hypoxia and protein amidation, while centriole-centriole adhesion displays an antagonistic function compared to non-recurrent patients
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1343 THE GUT MICROBIOTA PROFILE AND HOST ANTI-MICROBIAL RESPONSE AT ONSET OF ULCERATIVE COLITIS IS ASSOCIATED WITH DISEASE COURSE

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**Introduction:** The clinical disease course of ulcerative colitis (UC) is unpredictable; some patients have mild symptoms whereas others suffer from frequent and severe flares and the reason for this is unknown. The gut microbiota and the host immune defense are key players for gut homeostasis and may be linked to disease severity.
**Aims & Methods:** Our aim was to determine the gut microbiota profile and mucosal anti-bacterial response in newly diagnosed patients with UC and correlate these data to disease course during the first three years. To do this we obtained rectal biopsies and fecal samples at onset of the disease from 44 therapy-naïve patients with UC. Patients were followed for 3 consecutive years and disease severity was assessed annually. Patients defined as having a mild disease course had ≤1 flares per year, whereas patients with a relapsing disease course had >1 flare per year at least one of the three years during follow-up. Microbiota analysis of fecal samples was performed for patients where fecal samples were present using the GA-map™ Dysbiosis Test (Genetic Analysis AS, Oslo, Norway). Gene expression in biopsies was analyzed by RT$^2$ Profiler PCR array for 84 genes involved in "Anti-bacterial response" (Qiagen) and confirmed by regular quantitative rtPCR. Multivariate factor analysis using orthogonal partial least squares discriminant analyses (OPLS-DA) (SIMCA-P+ software; Umetrics, Umeå, Sweden) was used to examine the relationship between bacterial content and mRNA expression to disease severity. The quality of the OPLS-DA was based on the parameter R2, defining the goodness of the fit of the model (good fit R2 > 0.5, best possible fit, R2 = 1).
**Results:** No demographic or disease specific parameters at disease onset discriminated between patients having mild (n = 23) or relapsing (n = 21) disease. Microbiota analysis of fecal samples (relapsing n = 11, mild n = 7) revealed differential clustering between the groups for the total set of bacteria (R2 = 0.55). However, no significant differences for bacterial species of phyla were found. Exploratory mRNA array analysis performed for a subset of patients (mild n = 5, relapsing n = 8) to get an insight into the mucosal anti-bacterial response showed distinct discrimination between the groups (R2 = 0.87). Bactericidal/permeability-increasing protein (BPI) and chemokine (C-X-C motif) ligand 2 (CXCL2) were the most important nominators for the discrimination. These data were confirmed in a larger cohort of patients and showed that BPI was increased (0.0002 (0.0001–0.0004) vs. 0.00009 (0.00005–0.0002), (median (IQR), p < 0.0001) and CXCL2 decreased (0.091 (0.048–0.154) vs. 0.119 (0.102–0.217), p = 0.02) in patients with mild disease vs. patients with a relapsing disease course (mild n = 23, relapsing n = 21). BPI levels correlated negatively to the total numbers of flares during the three years (r = -0.52, p = 0.0003).
**Conclusion:** The mucosal anti-bacterial response in patients with newly diagnosed UC is associated to the disease course during follow-up. This indicates that patients with a non-favorable anti-microbial expression pattern could benefit from an intensified treatment regime.
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L. Öhman: Unrestricted research grants from AstraZeneca; Consultant/ Advisory Board member for Genetic Analysis; Speaker for Genetic Analysis, Takeda and Abbot.
All other authors have declared no conflicts of interest.

## P1344 THE ROLE FOR T CELLS IN THE PATHOGENESIS OF CROHN'S DISEASE-ASSOCIATED FISTULAE

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**Introduction:** Fistulae represent a frequent complication in Crohn's disease (CD). Surgical intervention is often required, as medical treatment outcome with conventional drugs is frequently insufficient. We have previously demonstrated that epithelial-to-mesenchymal transition (EMT) plays a critical role for fistula development. The cytokines tumor necrosis factor (TNF), interleukin (IL)-13, interferon (IFN)$\gamma$, IL-17 A and IL-22 are highly expressed in transitional cells along fistula tracts in CD patients. Similar to transforming growth factor (TGF) $\beta$, TNF is able to induce EMT and the expression of molecules being associated with cell invasiveness and migration. IL-13 induces expression of genes being associated with invasive cell growth, such as SLUG transcription factor and $\beta$6-integrin. Here, we analyzed the implication of the T cell-derived cytokines IFN$\gamma$, IL-17 A and IL-22 in the event of EMT. Moreover, we investigated if there are differences in the composition of lymphocytes in the blood of CD patients suffering from fistulae compared to patients without fistulae or healthy controls.
**Aims & Methods:** Three-dimensional intestinal epithelial cell (IEC) constructs (spheroids) were stimulated with IFN$\gamma$, IL-17 A and IL-22 to investigate the effects on EMT development. Further, CD4+ and CD25+ T cells were isolated from fistulizing CD patients' blood or control blood samples and co-cultured together with HT29 cells. Afterwards, mRNA expression levels of EMT-associated genes were analyzed.
**Results:** Treatment of the spheroid model with IFN$\gamma$ resulted in a loss of the well-defined globular spheroid shape after day 7. We observed a clear separation of IECs, while mRNA levels for EMT-related transcription factors like SNAIL-1 and ETS-1 were not up-regulated. IL-17 A and IL-22 had no effect on cell morphology suggesting that they do not induce EMT in our cell model. On a molecular level, both cytokines had no effect on the mRNA expression of EMT-associated genes, but prevented the TGF$\beta$-induced up-regulation of e.g. SNAIL-1 or ETS-1. The sorting of T cells isolated from blood of CD patients with fistulae revealed an elevated expression level of CD4+ and CD25+ T cells compared to healthy controls.
**Conclusion:** Our data demonstrate that T cell derived cytokines may play a crucial role in the pathogenesis of CD-associated fistulae. Th1 cell-derived IFN$\gamma$ may be involved in the event of EMT in IECs, however Th17 cell-derived cytokines IL-17 A and IL-22 are likely not implicated in EMT onset, and may prevent EMT-associated effects of TGF$\beta$. This observation supports the hypothesis that Th17 cell-derived cytokines exert a pivotal role for maintaining intestinal homeostasis. The different lymphocyte composition in CD patients' blood represents a further hint for the importance of these cells in fistulae formation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1345 CAN TISSUE AND PERIPHERAL EOSINOPHILIA BE USED AS PREDICTORS FOR DISEASE OUTCOME IN CHILDREN WITH ULCERATIVE COLITIS?

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**Introduction:** Eosinophils are implicated in the pathogenesis of ulcerative colitis (UC).
**Aims & Methods:** To evaluate the magnitude of mucosal and blood eosinophils in newly diagnosed pediatric UC patients and to investigate its clinical significance in predicting the long-term disease outcome.We retrospectively evaluated colorectal biopsies of 96 patients. Samples were taken from diseased areas of the colon and examined by a gastrointestinal pathologist. The most inflamed site was used for assessment of mucosal eosinophils. Demographic data, disease characteristics and long-term outcomes were extracted from medical charts. Associations between histologic features and clinical outcomes were analyzed.
**Results:** Samples from 96 diagnostic colonoscopies as well as 70 follow-up colonoscopies (49 patients) were evaluated. Median age was 13.3 years (IQR 10.1–15.3). Median duration of follow-up was 12.8 years (IQR 7.2–17.1). Median number of tissue eosinophils at diagnosis was 45 (IQR 22–73) compared to 10 eosinophils (IQR 8–25) during histologic remission (p < 0.0001). Peripheral absolute eosinophil counts correlated significantly with tissue inflammation (p = 0.001) and with tissue eosinophilia (P = 0.001). Severity of

both mucosal eosinophilic infiltration ($p = 0.02$) and peripheral eosinophilia ($p = 0.04$) was associated with clinical severity of UC at diagnosis. Multiple logistic regression analysis showed that severe eosinophilic infiltration is associated with corticosteroid therapy following diagnosis ($p = 0.04$) but not with a long-term risk for step-up therapy or colectomy.
**Conclusion:** Tissue and peripheral eosinophilia in pediatric UC patients correlate with disease severity at diagnosis and with the risk for corticosteroid requirement following diagnosis. However, for our cohort, these did not serve as predictors for poor long term outcome including colectomy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1346 IL-33/ST2 AXIS SUSTAINS GUT MUCOSAL WOUND HEALING AND CANCEROGENESIS IN COLITIS-ASSOCIATED COLORECTAL CANCER

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**Introduction:** IL-33 and its receptor, ST2, are important factors in IBD pathogenesis. Emerging evidence also suggests its potential role in epithelial proliferation inflammation-driven tumorigenesis.
**Aims & Methods:** To characterize the precise contribution of IL-33/ST2 axis in the DSS and AOM/DSS model of colitis. C57/BL6 wild-type (WT), IL-33 KO and ST2 KO mice were given a single dose of AOM and two cycles of 3% DSS for 7 d. Body weight, occult blood test, and stool consistency were measured to calculate the Disease Activity Index (DAI), and endoscopic and histological evaluation of colons were performed. Aged-matched WT mice, injected with vehicle and given regular drinking water were used as controls (CT). At 8 wks post AOM injection mice were sacrificed. IHC, immunofluorescence (IF) and qPCR were done on full-thickness colons for IL-33 and ST2 localization and identification, and mRNA expression. FACS analysis was performed on resected, isolated polyps in order to functionally characterize ST2+ cells. Moreover, in order to characterize the precise role of the IL-33/ST2 axis following acute epithelial injury and mucosal repair, 3% DSS was administered for 5 d to C57/BL6 WT, IL-33 KO and ST2 KO mice. DSS was then replaced with drinking water for 2 wks (recovery period). Another group of WT mice received DSS for 5 d and IL-33 or vehicle (VEH) every other day during the recovery period. Mice were sacrificed either after DSS challenge or after 1 or 2 wks of recovery.
**Results:** In AOM/DSS models, IL-33, ST2L, and sST2 mRNA transcripts were dramatically elevated in WT vs. CT mice. IHC of treated WT mice revealed localization of IL-33 to the colonic epithelium and to cells within the LP morphologically consistent with tissue macrophages. ST2 staining was localized to the intestinal epithelium in tissues immediately adjacent to tumors, while within the tumors themselves, ST2+ cells displayed a spindle/fibroblast-like morphology with a unique distribution throughout the polyps. Little to no staining for both IL-33 and ST2 was present in CT. Using IF, ST2 co-localized with αSMA in polyps; however, ST2 staining was not exclusive for αSMA+ cells. FACS analysis showed a distinct population of CD45+ hematopoietic cells consisting of CD3/CD8+ cytotoxic T cells (CTLs), CD19+ B-lymphocytes, CD11b+CD11c- and CD11b+CD11c+ myeloid cells. ST2 was mainly expressed by CTLs, and CD11b+CD11c- and CD11b+CD11c+ myeloid cells. Non-hematopoietic cells (CD45-) also expressed ST2. DSS challenge in WT mice resulted in increased body weight loss and DAI vs. IL-33 KO and ST2 KO mice. At 5 weeks post AOM injection, experimental mice underwent survival colonoscopy. WT had already developed protruding lesions with abnormal vascular patterns, suggesting pre-tumorous lesions, while IL-33 KO and ST2 KO mice showed the absence of pre-tumorous lesions with a more impressive mucosal inflammation, likely due to reduced epithelial proliferation and repair caused by the absence of IL-33 signaling. At sacrifice, increased number and size of polyps were observed in WT vs. IL-33KO and ST2KO mice. In DSS model, more severe colitis was observed following DSS+1wk recovery vs. after 5 d of DSS, which decreased after DSS+2wks recovery. ST2 staining was more evident during the recovery phase following DSS, notably localized to subepithelial myofibroblasts in close proximity to areas of re-epithelialization. Both IL-33 and ST2 KO mice showed increased colonic inflammation after 2 wks recovery compared to after 5 d DSS and vs also WT. IL-33 treatment of WT mice resulted in increased body weight, reduced DAI, and decreased colonic inflammation after 2 wks recovery vs. VEH.
**Conclusion:** Our results suggest that activation of the IL-33/ST2 axis sustains mucosal healing promotes epithelial repair and mucosal healing following acute epithelial injury during DSS-induced colitis. On the other side, it is also crucially involved in tumorigenesis in the murine model of colitis-associated CRC. Further studies are underway to determine mechanisms of action that support these findings.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1347 CEACAM1 REGULATION OF BCR SIGNALING IN THE ACTIVATED B CELLS

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**Introduction:** It has been recently shown that the carcinoembryonic antigen-related adhesion molecule 1 (CEACAM1) expressed in T cells may regulate immune responses in the gut.[1,2] In addition to T cells, B cells are also one of the major populations in the gut-associated lymphoid tissue that orchestrates mucosal homeostasis. However the role of CEACAM1 in B cells has not been elucidated.
**Aims & Methods:** We analyzed B cell subsets in the lymphoid tissues of wild type C57BL6 mice as well as a murine B cell line, A20, to determine the expressions and functions of CEACAM1.
**Results:** FACS analysis of the lymphocyte subsets isolated from lymphoid tissues such as spleen, mesenteric lymph nodes and Peyer's patches of C57BL6 revealed that CEACAM1 expression on B cell surface was more than that of T cells. Bone marrow analysis showed that the expression level of CEACAM1 was increased during maturation and differentiation process of B cells. When splenic B cells were stimulated with either LPS, anti-CD40, or anti-m chain antibodies (Abs) in the presence or absence of agonistic anti-CEACAM1 Ab, the increased cytokine production such as IL-4 and IL-5 by activation via B cell receptor (BCR) signaling was specifically suppressed by CEACAM1 signaling rather than B cell activations via either TLR4 or CD40 signaling. Immunofluorescent studies revealed that the expression of CEACAM1 aggregated and co-localized with BCR expression under the confocal microscope when B cells were activated with anti-m chain Ab. Given these results, A20 cells were transfected with CEACAM1 cDNA. Immunoblotting showed that the overexpression of CEACAM1 suppressed BCR signaling in these cells when compared to that of vector alone-transfected control. Moreover, the overexpression of CEACAM1 in these cells resulted in reduced expressions of activation markers such as CD69, CD80, CD86, MHC-1 and -2 on the cell surface. These observations were associated with decreased $Ca^{2+}$ influx and suppressed cytokine production by the overexpression of CEACAM1 after BCR signal activation.
**Conclusion:** These results suggest that CEACAM1 may regulate B cell activation and differentiation specifically via BCR signaling.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1348 METABONOMICS REVEALS DISTINCT SERUM METABOLIC CHANGES DURING INFLIXIMAB THERAPY OF INFLAMMATORY BOWEL DISEASE

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**Introduction:** Few studies have focused on identifying predictive response biomarkers in patients with inflammatory bowel disease (IBD) treated with infliximab (IFX)[1,2]. With the advent and feasibility of proton nuclear magnetic resonance ($^1$H NMR) spectroscopy-based metabolic profiling[3,4] of serum in IBD, metabonomics presents itself as an obvious tool for differential diagnostics and identification of predictive response biomarkers
**Aims & Methods:** This study aims at performing a longitudinal cohort study of $^1$H NMR spectroscopy-based metabolic profiling of serum from IBD patients treated with IFX 1) to substantiate the potential use of spectroscopy as a semi-invasive diagnostic tool, 2) to provide insight into the disordered metabolism during active and quiescent IBD, and 3) to identify metabolic changes during treatment with IFX in order to explore markers of favorable outcomes. Successive serum samples collected during IFX induction treatment (weeks 0, 2, 6, and 14) from 87 IBD patients and 37 controls were analyzed by $^1$H NMR spectroscopy. Patients were divided into three different response types in accordance with disease activity at 14 weeks: Remission (Mayo score $< 2$, Harvey Bradshaw (HB) score $< 5$, and/or PDAI score $< 5$), Responder (reduced Mayo score, HB score, and/or PDAI score, but Mayo score $\geq 2$, HB score $\geq 5$, and/or PDAI score $\geq 5$), and Non-responder (no clinical response). Data were analyzed with principal component analysis and orthogonal-projection to latent structure-discriminant analysis using SIMCA-P+ 12 and MATLAB.
**Results:** The metabolic profiles were significantly different between active ulcerative colitis (UC) vs. controls; active Crohn's disease (CD) vs. controls, and quiescent CD vs. controls. The metabolites holding differential power primarily belonged to a range of lipids and phospholipids with pro-atherogenic characteristics, and metabolites involved in the pyruvate metabolism suggestive of an

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Significant up and down-regulated metabolites

| Metabolites | CD(0)vs. Control | UC(0)vs. Control | CDRem(0)vs. Control | CDRem(2)vs. Control | CDRem(6)vs. Control | CDRem(14)vs. Control | UCRem(0)vs. Control | UCRem(2)vs. Control |
|---|---|---|---|---|---|---|---|---|
| Valine | ↓ | ↓ | ↓ | ↓ | ↓ | — | — | ↓ |
| Glutamine | ↓ | ↓ | ↓ | ↓ | ↓ | — | — | ↓ |
| Glycine | ↓ | ↓ | ↓ | ↓ | ↓ | — | — | — |
| Histidine | ↓ | ↓ | — | — | — | — | — | — |
| Phenylalanine | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ |
| Lactate | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | — |
| Glucose | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | — | — |
| Pyruvate | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ |
| Formate | ↓ | ↓ | ↓ | — | — | — | — | — |
| Scyllo-inositol | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |
| NAG | ↑ | ↑ | ↑ | — | — | — | — | — |
| GPC | ↓ | ↓ | ↓ | ↓ | — | — | — | — |
| HDL | ↓ | ↓ | ↓ | ↓ | ↓ | — | — | — |
| VLDL | ↑ | ↑ | — | ↑ | ↑ | — | — | — |
| U1 | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ |

CD, Crohn's disease; GPC, glycerophosphocholine; HDL, high density lipoprotein; NAG, N-acetyl glycoprotein; Rem, remission; U1, unknown metabolite; UC, ulcerative colitis; VLDL, very low density lipoprotein (0), before 1st infusion of infliximab at week 0; (2), before 2nd infusion at week 2; (6), before 3rd infusion at week 6; (14), before 4th infusion at week 14 ↑ increased or ↓ decreased compared to controls

intense inflammation-driven energy demand. All remaining models were insignificant including the models comparing different IFX treatment response types, i.e. remission, responder, and non-responder, as well as successive serum samples across the duration of induction within each of these response types.
**Conclusion:** In conclusion, $^1$H NMR spectroscopy-based metabonomics on successive serum samples from patients with IBD has proven to be a potentially powerful semi-invasive diagnostic tool in flaring UC and CD providing unique insights into the metabolic changes taking place during induction treatment with IFX. No applicable response biomarkers could be identified, but the identification of a reversible pro-atherogenic lipid profile in IBD patients with active disease might be of clinical importance in terms of statin treatment of IBD patients with continuous inflammation or frequent flares.
**Disclosure of Interest:** C. Steenholdt: Within the last 2 years, C Steenholdt has served as speaker for Abbvie, Pfizer, and MSD; and consultant for Pfizer and Takeda Pharmaceuticals
All other authors have declared no conflicts of interest.

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### P1349 IDENTIFICATION OF A TRANSCRIPTIONAL SIGNATURE ASSOCIATED WITH POST-OPERATIVE RECURRENCE IN CROHN'S DISEASE: A STUDY FROM THE REMIND GROUP


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**Introduction:** Post-operative recurrence is a major concern in Crohn's disease (CD).
**Aims & Methods:** The aim of this study is to identify a molecular signature associated with post-operative recurrence in the neo-terminal ileum and the biological pathways associated. The REMIND Post-operative study has been performed in 9 centers of the REMIND group, collecting data at time of surgery and of endoscopy (performed at 6 months), associated with an extensive bio-banking. Clinical, biological and endoscopic parameters (description and location of elementary lesions, Rutgeerts score) were collected at month 6. Endoscopic recurrence was defined by a Rutgeerts score$\geq$1. Baseline factors (demographic and phenotypic variables) associated with endoscopic recurrence were searched by univariate and multivariate regression analysis. Biopsies of ileal mucosa were collected on surgical specimen and by endoscopy six months after surgery. Whole genome expression analysis was performed using microarray study and followed by Gene Ontology and clustering analyses.
**Results:** Thirty patients representative of the whole REMIND cohort were selected: 53% were male, median age at surgery was 30 years old. One third of patients (33%) were active smoker at time of surgery. Twenty patients (66.6%) received pre-operative anti-TNF therapy, while 10 (33%) received anti-TNF after surgery. Nineteen (63%) patients had an endoscopic recurrence as defined by a Rutgeerts score$\geq$1. Principal component analysis (PCA) showed two clusters of patients according to their transcriptional profiles, which highly correlated with post-operative recurrence. Indeed in the first cluster, 12 patients out of 13 had endoscopic recurrence; while 10 out of 17 patients had no endoscopic recurrence in the second cluster. Endoscopic recurrence was associated with significant regulation of inflammatory genes such as S100A8, S100A9, IL1B, IL6, CCL2, CCL8 and GZMA. Remarkably, the molecular signature of non-recurring patients was not similar to non-IBD healthy controls (ileal biopsies; n = 9). Moreover, study of samples at time of surgery defined different types of transcriptional profiles.
**Conclusion:** This study revealed a correlation between gene expression profiling and recurrence of mucosal inflammation after surgery in CD. Analysis of the whole data set (in progress) could lead to the identification of important pathways involved in post-operative recurrence in CD.
**Disclosure of Interest:** M. Allez: I received honoraria from MSD, Abbvie, Janssen, UCB, Takeda, Ferring, Novartis, Pfizer, Genentech
All other authors have declared no conflicts of interest.

### P1350 ANTI TNFA THERAPY MODULATES THE INTESTINAL MICROBIOTA ACROSS CHRONIC INFLAMMATORY DISEASE


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**Introduction:** Immune modulating antibodies targeting a specific cytokine signal (e.g. TNF-$\alpha$, IL-6) are the mainstay in therapeutic control of a broad and heterogeneous group of chronic inflammatory diseases, including rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). Pathogenesis of these diseases is argued around microbial driven activation of immune cascade and cytokine imbalance; however the impact of such targeted cytokine blockade on intestinal microbial communities is poorly understood.

**Aims & Methods:** This study aims to determine the impact of anti TNFa therapies on microbiota in patients with rheumatoid arthritis and with inflammatory bowel disease. We enrolled patients with RA (n = 38) and IBD (n = 14) and healthy volunteers (n = 24) for this longitudinal study. Patients enrolled were naïve to previous biological therapy. Fecal samples were collected at baseline of therapy induction and on 1 day, 3 day, 1 week, 1 month and 6 months of therapeutic interventions. DNA was extracted from fecal samples and V4 region of the 16 S rRNA gene was sequenced using MiSeq Illumina platform.
**Results:** Compared to healthy control, IBD and RA patients display a specific microbial pattern of luminal gut microbiota at baseline. Moreover, in response to therapy induction we observed significant differences in the proportion of major bacterial groups (*Firmicutes* and *Actinobacteria*) in a time dependent manner. Likewise microbial composition and structure (beta diversity) was significantly altered after therapy if compared to the changes in healthy volunteers within same time frame. The observed microbial changes could not specifically attributed to TNFa inhibition in different disease types but rather seemed to reflect the overall changes of systemic immunity in response to therapy induction
**Conclusion:** Our data suggests a marked influence of biological therapies on microbial composition and structure, irrespective of underlying disease.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1351 GAMMADELTA T CELL DEFICIENCY IN THE PERIPHERAL BLOOD OF PATIENTS WITH CROHN'S DISEASE: RELATIONSHIP WITH CLINICAL AND ENDOSCOPICAL ACTIVITY

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**Introduction:** Crohn's disease (CD) is a chronic relapsing systemic disease affecting the gastrointestinal tract. An altered immune reponse to commensal intestinal bacteria takes place in genetically predisposed individuals, and it can be considered an immune deficiency condition. Gamma delta T lymphocytes (GDTL) are considered key cells in the first line of defense against infections and can stimulate wound healing. Murine studies have shown their protective role against colitis in IBD models. Their clinical role in CD pathogenesis and prognosis is largely unknown.
**Aims & Methods:** We aimed to determine the numbers of GDTL in the peripheral blood (PB) of a large cohort of CD patients and matched controls and study its relation with the clinical and endoscopical activity. A prospective study of 102 patients with CD compared with 102 healthy subjects (control group) matched by age and sex was undertaken. Lennard-Jones criteria were used for the diagnosis of CD. Disease activity was measured with the Crohn's disease activity index (CDAI) and endoscopical activity by the SES-CD index. New patients, patients in remission, and patients with active disease were evaluated. Lymphocytic populations of CD3+, CD4+, CD8+, CD56+, and $\alpha\beta$ and $\gamma\delta$ subsets were measured in the PB of all participants.
**Results:** The number of total CD3+, CD4+, CD8+ and CD56+ lymphocytes was decreased in CD patients compared with the control group ($p < 0.001$, 0.003, $<0.001$, and 0.001, respectively). Although both $\alpha\beta$ and $\gamma\delta$ T lymphocytes were lower in patients, GDTL subsets showed the lowest levels in CD patients (mean 0.0332 x $10^9$/l) vs controls (mean 0.0753 x$10^9$/l), $p < 0.001$. This decrease was significant for both CD4+$\gamma\delta$, CD8+$\gamma\delta$ and CD56+$\gamma\delta$ subsets ($p < 0.001$), and for all the clinical scenarios studied (new patients, remission or active disease) $p < 0.001$. In addition, we found and inverse correlation between the numbers of CD3 + $\gamma\delta$ and CD8 + $\gamma\delta$ (and not the $\alpha\beta$ T lymphocytes) with the clinical (-0.304 and -0.249; $p = 0.014$ and $p = 0.017$ respectively) and endoscopical activity (-0.275 and -0.249; $p = 0.017$ $p = 0.017$).
**Conclusion**: This study confirms a decrease in the global lymphocyte population in the peripheral blood of patients with CD. This decrease is more evident in gamma-delta T lymphocytes. Our results show for the first time an inverse correlation between GDTL numbers in PB and disease activity, highlighting the importance of these cells in the pathogenesis of the disease with potential therapeutical implications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1352 INTESTINAL TOTAL BACTERIA CONCENTRATION AND TRANSLOCATION OF BACTERIA AT THE INFLAMMATORY BOWEL DISEASE

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**Introduction:** The gut microbiota is believed to play a central role in the development of the inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC). Recently has been suggested that live commensal intestinal bacteria are present in the adipose tissue and the peripheral blood where they can induce inflammation. Since this process can trigger inflammation the aim of the present study was to evaluate the intestinal bacteria concentration and translocation of bacteria in IBD.
**Aims & Methods:** Both blood and tissue biopsy samples were collected from children (n = 6) and adult patients with active CD (n = 3) and UC (n = 6), as well as from healthy individuals (n = 9) underwent screening colonoscopy. Most of the patients were newly diagnosed and none of them received antibiotics. All of the adults received 5-ASA and three of them anti-TNF. Samples were taken before starting and after 12–20 weeks of anti-TNF treatment. For each samples (tissue and blood) the purified DNA was eluted and analyzed for total bacteria using suitable primers targeting 16S rRNA gene by Real-Time PCR. Reference microbial strain E.coli used for standard curve construction. Total tissue and blood bacterial DNA were determined by interpolating the Ct values obtained from the samples into the appropriate standard curve.
**Results:** The total bacterial count was similar in tissue biopsies and blood samples. However, adult UC patients had increased bacterial count ($87.02 \pm 1.02$ ng/ul in tissues and $84.53 \pm 0.5$ ng/ul in blood) compared to CD ($74.58 \pm 0.52$ ng/ul in tissues and $75.55 \pm 0.51$ ng/ul in blood) ($p < 0.05$). In children samples bacterial count, in both tissue ($48.38 \pm 7.74$ ng/ul) and blood ($49.15 \pm 5.89$ ng/ul) samples, was significantly lower than adult's samples ($p < 0.001$). In all cases adult and children patients, the bacterial count was significantly higher than in controls ($34.02 \pm 0.03$ in tissues and $43.1 \pm 0.14$ ng/ul in blood) ($p < 0.001$). Interestingly, when we compared the samples of patients who received anti-TNF treatment before and after the treatment we shown that the bacterial count diminished significantly after anti-TNF treatment, in the levels to control samples in both tissues (before anti-TNF $81.4 \pm 9.4$ vs after anti-TNF $29.43 \pm 6.54$ ng/ul, $p < 0.01$) and blood samples (before anti-TNF $80.12 \pm 6.33$ vs after anti-TNF $50.32 \pm 7.03$ ng/ul, $p < 0.01$).
**Conclusion:** Our results idicate the translocation of bacteria from gastrointestinal system in the circulation in IBD cases and the bacterial count in bloodstream could be a less invasive indicator of response to anti-TNF treatment. Further studies to identify the bacterial species in this cases are in process.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1353 ANALYSIS OF MACRONUTRIENTS INTAKES IN INFLAMMATORY BOWEL DISEASE: CORRELATION WITH DISEASE ACTIVITY

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**Introduction:** The pathogenesis of inflammatory bowel disease (IBD) is complex, with multiple interactions between genetics, infections, microbiota and diet. Diet pattern has been observed as a possible environmental trigger for IBD. On the other hand, the activity of the disorder may affect dietetic intake. Therefore, we evaluated diet macronutrients in IBD and correlated them with disease activity.

**Aims & Methods:** A hundred and fifty IBD patients (84 Crohn's disease-CD and 66 ulcerative colitis-UC) and 100 healthy volunteer controls were enrolled. All patients answered a 24-hour recall questionnaire/personal interview to evaluate macronutrient intakes (total calories, carbohydrates, refined sugars, lipids, proteins, total fibers, insoluble/soluble fibres). Data were elaborated by a dedicated software (WinFood). Disease activity was estimated by global Mayo and Harvey Bradshaw index-HBI. We evaluated the association of dietetic factors with disease activity as well as with immunomodulator or biologic therapy using both univariate and multivariate analysis with linear regression.
**Results:** We did not observe any difference in total calories, proteins and carbohydrates intake among controls, IBD receiving immunomodulators and IBD under biologics. Controls assumed less lipids in diet than patients with IBD and more fibres, both soluble and insoluble. For CD, HBI score was directly correlated to carbohydrate intake ($b = 6.752 \pm 3.25$, $p = 0.04$), however the multivariate analysis did not confirm this finding ($b = 0.65 \pm 1.12$, $p = 0.26$). For UC, the disease activity directly correlated with total caloric intake ($b = 2.72 \pm 1.7$, $p = 0.008$) and inversely with carbohydrates ($b = -3.02 \pm 2.53$, $p = 0.03$), and multivariate analysis confirmed such findings both for carbohydrates ($b = -1.1 \pm 0.17$, $p = 0.03$) and total calories ($b = 1.19 \pm 0.04$, $p = 0.049$). Type of drug medications was not a confounding factor in the correlation between dietary intakes and disease activity.
**Conclusion:** We found that the assumption of carbohydrates Is correlated with disease activity directly for CD and inversely for UC. Mayo score was then directly correlated to total caloric intake in UC. A direct cause-effect relationship cannot be demonstrated by our study since the study does not allow to establish whether the diet affects the disease or the disease affects dietetic habit.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1354 IN DEPTH RESEARCH ON AIEC STRAINS RECOVERED FROM CROHN'S DISEASE PATIENTS AND THEIR HEALTHY RELATIVES: A RISK FOR INTRAFAMILIAL TRANSMISSION?

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**Introduction:** Intrafamilial cases of Crohn's disease (CD) are well documented; they may be linked to genetic susceptibility and/or transmissible agents. Adherent-invasive *E. coli* (AIEC) has been consistently implicated as a pro-inflammatory species in CD.
**Aims & Methods:** The aim of our study was to investigate similarities between different *E. coli* strains isolated from stools of CD cases and their healthy relatives issued from a French population-based CD registry. 246 strains from 38 individuals belonging to 17 families with at least one case of CD were checked for invasive ability by infecting Intestine-407 (ATCC CCL-6) epithelial cells during three hours by the E.coli strains at a multiplicity of infection of 10 bacteria per cell. After cell-rinsing by PBS (3 times), fresh medium containing 100 $\mu$g/mL of gentamicin was added and further incubated for 1 hour (in order to kill extracellular bacteria). The cells were then lysed with 500 $\mu$L of 1% Triton X-100 and intracellular bacteria are outnumbered. The isolates were considered invasive when (intracellular bacteria / initial inoculum) $\times$ 100 was $\geq$0.1%. Two controls were systematically tested, a non-invasive *E. coli* strain (K12 C600) and the AIEC reference strain LF82. Strains belonging to the AIEC pathovar were further typed by Pulsed Field Gel Electrophoresis (PFGE) using XbaI as restriction enzyme.
**Results:** A total of 82 AIEC strains from 38 individuals (19 CD patients and 19 healthy relatives) belonging to 17 families were isolated. They generated 71 different PFGE profiles, indicating a high variability both in patients and their healthy relatives. One person can harbor up to three different profiles of AIEC strains.
**Conclusion:** The AIEC population is rather heterogeneous and different AIEC profiles can be found in the same sample. On the whole profiles are different in healthy persons and CD patients belonging to the same family. These observations are in agreement with a low risk or intrafamilial transmission. Financial support: This work was supported by the SATT (Sociétés d'Accélération du Transfert de Technologies).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1355 IMPROVEMENT OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC INFLAMMATORY BOWEL DISEASE AFTER 4 WEEKS OF ADDITIVE TREATMENT WITH MENTHACARIN – A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

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**Introduction:** Since the early 1950s, a rise in the incidence of inflammatory bowel disease (IBD) has been observed. In Western Europe, IBD affects 0.5–1.0% of the population during their lifetime[1]. The main symptoms of IBD are diarrhea in connection with stools containing blood and mucus as well as pain and abdominal cramps. The most common types of IBD are ulcerative colitis and Crohn's disease. We analyzed data from a prospective, randomized, placebo-controlled, double-blind, parallel-group, multi-center clinical trial in outpatients with IBD, defined here as ulcerative colitis and Crohn's disease. The results of health-related quality of life (QoL) in patients with chronic inflammatory bowel disease after 4 weeks of additive treatment with Menthacarin* will be reported here.
**Aims & Methods:** The trial was performed by 27 internists, gastroenterologists, and general practitioners in Germany. In total, 135 male or female, adult outpatients suffering from IBD were randomized and treated for 4 weeks with Menthacarin capsules or placebo (2 x 1 capsule/day) - as an additive treatment. The patients' medication for treatment of IBD had to be administered in constant dosage. Baseline-values for health-related QoL, as rated by the patient using the validated 'Inflammatory Bowel Disease Questionnaire' (IBDQ)[2] were compared with QoL-results at the end of trial.
**Results:** There was an improvement in the total score of IBDQ by $25.6 \pm 30.2$ points (from $149.1 \pm 24.1$ to $175.8 \pm 24.6$ points) under Menthacarin-treatment (full analysis set, mean $\pm$ SD; $n = 61$) compared to an improvement of $11.0 \pm 22.5$ points (from $149.4 \pm 32.4$ to $160.2 \pm 30.0$ points) in the placebo group (full analysis set, mean $\pm$ SD, $n = 64$). This results in a corresponding p-value of 0.0012 (full analysis set, U-test, one-sided). All the four dimensions of the IBDQ (bowel symptoms, systemic symptoms, emotional and social function) demonstrate the significant improvement in the Menthacarin-group compared to the placebo group as well.
**Conclusion:** Menthacarin significantly improved health-related QoL in patients affected by IBD and was well tolerated. _____ *Menthacarin® is a proprietary combination of essential oils of a specified quality from Mentha x piperita L. (90 mg Peppermint oil WS® 1340) and Carum carvi (50 mg Caraway oil WS®1520)
**Disclosure of Interest:** M.A. Engel: I received honoraria from Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe, Germany.
B. Stracke: I am an employee of Dr. Willmar Schwabe GmbH & Co. KG, Karlsruhe, Germany.

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## P1356 PROPHYLACTIC AND CURATIVE POTENTIAL OF THE HERBAL PREPARATION STW 5 IN AN EXPERIMENTAL MODEL OF CROHN'S DISEASE

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**Introduction:** STW 5 is a standardized multi-component herbal preparation consisting of extracts of bitter candy tuft, lemon balm, chamomile, Angelica, peppermint, milk thistle, caraway, celandine and liquorice. It has been used clinically in functional dyspepsia[1] and irritable bowel syndrome[2] and showed efficacy in experimental dextran sulphate induced colitis as a model of ulcerative coitis[3]. The present study was conducted to investigate its potential usefulness in 2,4,6 - trinitrobenzene sulfonic acid (TNBS) induced colitis as an established experimental model for Crohn's disease.
**Aims & Methods:** Colitis was induced by instilling TNBS in the colon of male Wistar rats under light ether anaesthesia. In a prophylactic setting, STW 5 was given orally1 week before induction of colitis and continued for 3 days after induction. Twenty-four hours later, rats were sacrificed. In the curative setting, STW5 was given orally 48 h after colitis induction daily for 1 week and the rats sacrificed 24 h later. Mucosal colonic damage was assessed macroscopically. Sulfasalazine was used as a reference drug. Colon homogenates and serum samples were used to assess levels of inflammatory and oxidative stress parameters. Immuno-histochemical staining of colon sections was used to assess calprotectin and IL-17 A levels, reported to be pertinent markers for IBD in man.
**Results:** TNBS colitis was evidenced by severe ulcerative damage, inhibition of reduced glutathione and a rise in myeloperoxidase in colon homogenates. Relevant cytokines TNF$\alpha$, IL-1$\beta$, ICAM-1 were elevated as well as LT-$B_4$

**P1357 Table1:** Cost of UC – 24 months prior to first NE admission to 24 months following first NE admission

| Age group | Cost of first admission | Admission post diagnosis | Outpatient gastroenterology | Inpatient endoscopy | Outpatient endoscopy | A&E gastroenterology |
|---|---|---|---|---|---|---|
| 0–15 | £278,009.21 | £55,316.54 | £254,193.76 | £184,155.33 | 0 | £6,291.61 |
| 16–30 | £1,791,556.72 | £2,771,071.82 | £1,116,013.46 | £1,184,373.75 | £13,640.77 | £58,800.8 |
| 31–50 | £3,341,371.68 | £3,010,543.24 | £1,251,378.49 | £1,212,658.85 | £18,713.65 | £51,713.99 |
| 51–75 | £5,779,692.95 | £4,789,813.5 | £1,100,563.6 | £1,612,289.53 | £21,181.86 | £62,492.72 |
| 75+ | £4,708,529.46 | £2,754,053.05 | £40,713.1 | £96,841.35 | £8,023.53 | £34,812.16 |

Total costs per patient per year were calculated using data from Table 1. For age group 0–15, this was £4,76.07. For ages 16–30, cost was £3,280.73. For ages 31–50, cost was £2,704.32. For ages 51–75, cost was £2,867.02 and for 75+, cost was £2,872.24. Patients below the age of 30 utilised more cost per patient than those above the age of 30.

and $PGE_2$. Immuno-histochemical examination showed a rise in calprotectin and IL-17 A. Pre-treatment with STW 5 prevented such effects in a similar manner to sulfasalazine. In the curative setting, STW 5 tended to normalize changes in reduced glutathione and myeloperoxidase and in ulcerative indices induced by TNBS.
**Conclusion:** Present findings provide good supportive evidence for the potential usefulness of STW5 in Crohn's disease.
**Disclosure of Interest:** O. Kelber: working for Steigerwald Arzneimittelwerk GmbH, Bayer consumer health
H. Abdel-Aziz: presently working for Steigerwald Arzneimittelwerk GmbH, Bayer Consumer Health
All other authors have declared no conflicts of interest.

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### P1357 THE TRUE COST OF ULCERATIVE COLITIS IN THE UK


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**Introduction:** Inflammatory Bowel Disease (IBD) has a prevalence of around 400 in 100,000 in the UK, with the prevalence of Ulcerative Colitis (UC) specifically of around 243 per 100,000. This gives a figure of 146,000 people in the UK living with UC. Around 30% of IBD patients are under regular hospital follow-up. Luces C et al found lifetime costs of IBD to be comparable to other major chronic illnesses such as heart disease and cancer.[1] In recent years there has been much focus on costs associated with new biologic agents for treatment of IBD. There are few studies looking at healthcare costs in terms of out patient assessments, admissions and diagnostics in Ulcerative Colitis. One recent Dutch study found healthcare costs of IBD to be stable over a 2-year period. [2] There are, in addition, inevitable costs incurred in the lead up to the eventual diagnosis of UC. This is a poorly researched area, which is likely to have a significant impact on total healthcare costs attributable to UC.
**Aims & Methods:** We aimed to determine the true costs attributable to UC over a 48-month period, spanning from 24 months leading up to the first non-elective admission for UC up to the 24 months following the first non-elective admission for UC. Hospital Episode Statistics data for 2011/2 for all clinical commissioning groups in England were analysed to calculate the cost of UC. The data used were obtained from the AXON Database, a health data warehouse that provides interrogative analysis and health intelligence on Hospital Episode Statistics (HES). Costs were calculated using national tariffs linked to Healthcare Resource Group (HRG) codes associated with each HES record. HES data from all the clinical commissioning groups in England for the year 2011 and 2102, 24 months up to the day prior to the first non-elective (NE) admission and 24 months following the first NE admission for UC were analysed. International Classification of Diseases – 10 (ICD-10) diagnosis codes related to UC were used to identify patients.
**Conclusion:** In the 48 months commencing 24months prior to the first NE admission for UC and ending 24 months after the first NE admission, there are significant costs in terms of admissions, outpatient assessments and diagnostics. Non-elective admissions, associated inpatient diagnostics in addition to attendance in A&E make up a high proportion of total cost. Non-elective care is often unplanned and more expensive than elective care. Better access to secondary care may reduce the cost burden of UC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1358 ENVIRONMENTAL FACTORS AND TRENDS IN IBD


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**Introduction:** The risk of developing inflammatory bowel disease (IBD) is dependent on the surrounding environment as a contributing factor. Smoking is associated with complicated Crohn's disease (CD), but it has a protective role in ulcerative colitis (UC). Processed food, caffeine and sugar intake are also likely to influence IBD.
**Aims & Methods:** All patients diagnosed with IBD between 2012 and 2014 at Mater Dei Hospital in Malta were included in this study as part of ECCO-EpiCom inception cohort. Each patient was then asked to fill in a questionnaire related to environmental factors.
**Results:** 152 patients (mean age 42.4 years SD ± 17.7; mean age at diagnosis 39.8 years SD ± 17.7) were included in this study. 55.9% were male. 65.8% patients suffered from UC.
Association of type of IBD with environmental factors: Patients with UC (38.1 years) had a mean older age at stopping smoking when compared to CD (30.3 years).($p < 0.027$) More UC patients were former smokers at the time of the study ($p < 0.01$) and at diagnosis ($p < 0.015$) and were ongoing smokers at diagnosis ($p < 0.033$). Whereas less UC patients were ongoing smokers at the time of the study ($p < 0.027$). Most patients with CD exercised daily or weekly. Most patients with UC exercised weekly or less. ($p < 0.013$) The higher the consumption of juices, the more likely the diagnosis of UC over CD. ($p < 0.007$) Patients with UC had an older mean age at the time of the study ($p < 0.003$) and at diagnosis ($p < 0.002$) and had a higher mean weight ($p < 0.001$) and BMI ($p < 0.007$).
Association of environmental factors with age at diagnosis: Patients with CD who had ever smoked ($p < 0.044$) and were exposed to passive smoking ($p < 0.032$) had a higher mean age at diagnosis than those who had never smoked and were never exposed to passive smoking. Those who were former smokers at diagnosis ($p < 0.008$) and at the time of study ($p < 0.026$) and those who smoked more than 20 cigarettes daily ($p < 0.008$) were older at diagnosis than. Those who had resumed smoking at diagnosis had a younger age at diagnosis.($p < .056$) CD patients on contraceptives ($p < 0.004$), those who consumed non-wholemeal bread ($p < 0.057$), those with the highest sugar consumption in coffee ($p < 0.01$) and tea ($p < 0.060$) and those who consumed most fast food ($p < 0.003$) had a younger age at diagnosis. Contrary to this, those with highest coffee ($p < 0.009$) and tea consumption ($p < 0.013$) were oldest at diagnosis. On constructing a general linear model, use of contraceptives ($p < 0.049$), consumption of fruit ($p < 0.022$), vegetables ($p < 0.033$), eggs ($p < 0.022$), bread ($p < 0.006$), cornflakes ($p < 0.014$), sugar in coffee ($p < 0.023$), sugar in tea ($p < 0.054$), fast food ($p < 0.030$), juices ($p < 0.048$), soft drinks ($p < 0.009$), tea ($p < 0.018$), pack years ($p < 0.028$) retained statistical significance. Patients with UC who had ever smoked ($p < 0.005$), were former smokers at diagnosis ($p < 0.0001$) and at the time of the study ($p < .0001$), smoked more than 20 cigarettes per day ($p < .029$) were older at diagnosis. Those with the highest consumption of fast food were youngest at diagnosis ($p < 0.001$). Those with the highest consumption of coffee ($p < 0.098$) and tea ($p < 0.024$) were oldest at diagnosis. On constructing a general linear model, pack years ($p < 0.001$) and total fast food ($p < 0.004$) consumption retained statistical significance.
**Conclusion:** A sedentary lifestyle, a higher consumption of juices and a higher BMI predispose to a diagnosis of UC. Smoking was protective in both UC and CD leading to an older age at diagnosis as was caffeine intake. Fast food consumption was also common to both types of IBD, leading to a younger age at diagnosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1359 IBD-RELATED MALIGNANCIES AND MORTALITIES OBSERVED IN 2015–2016. FIRST RESULTS FROM THE PROSPECTIVE NATIONWIDE HUNGARIAN REGISTRY

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**Introduction:** Inflammatory bowel diseases (IBD-Crohn's disease (CD); ulcerative colitis (UC)) are lifelong inflammatory conditions of the gastrointestinal tract. IBD-associated colorectal cancer (CRC) accounts for approximately 1–2% of all cases of CRC. Although data on mortality rates in IBD patients are controversial, CRC has been shown to account for approximately 10–15% of all deaths among IBD patients.

**Aims & Methods:** The aim of our nationwide registry was to prospectively collect IBD-related mortalities and all types of malignancies diagnosed in the Hungarian IBD population. Data on all death and malignancies developed from January 2015 in IBD patients were recorded. Each members of the Hungarian Society of Gastroenterology were prospectively interviewed 3 monthly by personal emails to report both death and malignancies observed in their patient population. Demographic and clinical data including previous immunosuppressive and biological therapy were also collected.

**Results:** Twenty-one newly diagnosed malignancies were reported (mean age: 48.2 years old, mean disease duration was 18.5 years; male/female ratio was 14/7) 14 CRC (mean age: 48.7 years, mean disease duration: 20.9 years, male/female ratio was 11/3; 1 pouch cancer previously colectomized because of sigmoid tumor), 1 with gallbladder, 1 with cervix, 1 with lung, 1 with esophagus, 1 with salivary gland, 1 with skin and 1 with tonsil cancer throughout the examined period. Eleven of the 14 CRC cases were associated with UC, 81% with pancolitis and chronic disease course. Eleven of the 14 cases were located on the rectosigmoid region, 2 had multiple localization (5 and 2 cancers simultaneously). Fifteen patients with treated IBD died during the examined period. Seven cases were related to IBD (5 males 2 females; 1 CD patient with rectal cancer, 1 patient with pouch cancer, 1 CD patient with interstitial pneumonia, 1 UC and 1 CD patients with septic complications, 1 UC patient with meningitis, 1 UC patient with hemorrhagic shock). Age of death was significantly lower in case of IBD-related mortality compared to the other patients and general population (44 vs. 65 vs. 73.4 (data from Central Statistical Office 2013, Hungary) years, $p = 0.02$). Immunosuppressive and/or biological therapy was ever given for 6 patients with IBD-related mortality.

**Conclusion:** The most frequently observed IBD-related malignancy is CRC, which can be multifocal and mainly involved the distal part of the colorectum typically in UC patients with pancolitis and chronic activity. Malignancy and septic complications were the leader causes of IBD-related mortality characterized by earlier death than in the rest and in the non-IBD population.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1360 CROHN'S DISEASE BEHAVIOR AND LOCATION IS ALTERED WHEN ASSOCIATED WITH PRIMARY SCLEROSING CHOLANGITIS

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**Introduction:** Primary sclorising cholangitis (PSC) is diagnosed in up to 7.5% of ulcerative colitis (UC) patients and less frequently (up to 3.4%) in Crohn's disease (CD) patients. The intestinal disease is usually milder but more extensive in patients UC-PSC patients compared to patients with no PSC. However, data on clinical characteristics of patients with PSC-CD are scarce. It has been suggested that CD-PSC patients have an extensive colonic involvement, leading in many cases to a diagnosis of indeterminate colitis. Classification of patients by phenotype is important for prediction of clinical outcome, tailoring therapy and for future understanding of disease pathogenesis, especially if they progress differently from isolated CD patients.

**Aims & Methods:** A retrospective case control analysis was performed on 18 patients with PSC and an established concomitant diagnosis of CD, who attended the IBD Center at the Tel Aviv Medical Center, between the years 2011–2014 (PSC-CD patients). PSC-CD patients were matched (by age, gender, and disease duration) to 90 CD patients (with no PSC) as controls. Disease phenotype (according to the Montreal classificaiton), demographic and clinical data were compared between the two groups. We aimed to clinically characterize Crohn's disease in patients who have concomitant primary sclerosing cholangitis.

**Results:** Disease in PSC-CD patients was more frequently limited to the colon (L2) compared to controls (50% vs 16%, $P = 0.004$). In contrast, a disease limited to the small bowel disease (L1) was noticed in only one PSC-CD patient as opposed to 30 of controls (6% vs 33%, $P < 0.05$). A non-stricturing-non-penetrating inflammatory phenotype was significantly more prevalent (83% vs 33%, $P = 0.0001$) in PSC-CD patients, while a penetrating phenotype (B3) was documented in only one patient with PSC-CD, signifacntly lower compared to controls (6% vs 33% $P < 0.05$). Use of 5-ASA agents as a single therapy was significantly more prevalent among PSC-CD patients compared to controls (39% vs 7% $P < 0.005$). In contrast, biologic therapy was significantly less common among PSC-CD patients compared to controls (17% vs 52%, $P = 0.0086$).

**Conclusion:** Patients with PSC-CD are clinically distinct from patients with isolated CD, and are characterized by a predominant colonic involvement and an inflammatory, non-stricturing-non-penetrating phenotype. These findings, if repeated in larger cohorts, may aid in strategising therapeutic interventions in these patients and in research of disease pathogenesis.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1361 THE BODY MASS INDEX DOES NOT INFLUENCE SUCCESS OF ANTI-TNFA THERAPY: RETROSPECTIVE SINGLE CENTER ANALYSIS OF 894 IBD PATIENTS

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**Introduction:** The course of inflammatory bowel disease (IBD) is highly heterogeneous. The available data on the impact of obesity in IBD patients is limited (1, 2). Therefore, we examined the impact of body mass index (BMI) on disease course and on therapeutic failure in a large single-center cohort of IBD patients treated with biological therapy.

**Aims & Methods:** We retrospectively analysed data from 894 IBD patients (60.4% Crohńs disease (CD); 39.6% Ulcerative Colitis (UC)) treated between 2002 and 2014 in the Department of Gastroenterology, University Hospital Münster. 317 (35.5%) patients received biological therapy with either Infliximab or Adalimumab (72.6% CD; 27.4% UC). Extent of disease, medical treatment and disease severity was analysed using Partial mayo score (UC patients) or Harvey-Bradshaw Index (CD patients), as documented in medical records. Bodyweight was categorized applying WHO definitions: underweight (BMI $< =18.49$), normal weight (BMI 18.5–24.99), overweight (BMI 25–29.99), and obesity (BMI $> 30$). Additionally, the time to therapeutic failure defined as new course of steroid treatment, escalation/change of medical therapy, hospitalization or surgery, was assessed. Statistical analyses performed were Kaplan-Meier estimator, Cox proportional hazards model and log-rank test.

**Results:** (1) Comparing BMI subgroups of all 894 patients, irrespective of disease severity or mode of therapy, overweight patients had a therapeutic failure latest (18 month, 95%CI: 10.4–25.6), followed by obese (14 month, 95%CI: 5.5–22.5) and normal/underweight patients (9 month, 95%CI: 6.4–11.6; Log Rank $P < 0.05$). To the contrary, an altered BMI was not predictive for an earlier or later therapeutic failure in the group of anti-TNF$\alpha$ treated patients: overweight patients failed after 24 month (95%CI: 12.5–35.5), obese after 19 month (95%CI: 0–38.5) and normal/underweight patients after 16 month (95%CI: 7.5–24.5; Log Rank $P = 0.76$). (2) Multivariate Cox regression of all IBD patients revealed BMI ($P = 0.04$), age at onset of disease ($P < 0.01$), nosologic entity ($P = 0.02$), and disease severity ($P < 0.01$) best predicted therapeutic failure; no associations regarding these variables were found in IBD patients treated with anti-TNF$\alpha$. (3) Assessing the time from start to therapeutic failure in Infliximab and Adalimumab-treated patients, no significant differences were detected between the two most commonly administered anti-TNF$\alpha$ antibodies.

**Conclusion:** In our large single-centre cohort study, BMI correlated strongly with therapeutic success in IBD patients, with rise in BMI reducing the risk of therapeutic failure. However, treatment success in the subgroup of anti-TNF$\alpha$ treated patients was not BMI-dependant. Prospective studies are warranted to further elucidate the impact of body weight on therapeutic success in IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1362 EFFECT OF INFLUENZA VACCINATION ON THE ACTIVITY OF INFLAMMATORY BOWEL DISEASE

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**Introduction:** Although influenza vaccinations are generally recommended by several guidelines in patients with inflammatory bowel disease (IBD) treated with immunosuppressive and/or biological therapy, the vaccination rate is low. This might be due to the fear of the potential negative effects of the vaccine on the activity of IBD.
**Aims & Methods:** The aim of the study was to assess the influence of the seasonal flu vaccine on the disease activity. Vaccination with the seasonal influenza vaccine was offered to patients. Stool samples were collected from each patient in order to detect calprotectin: one sample at the time of the immunization, and another one a month later. We recorded demographic and clinical data too.
**Results:** We enrolled 36 patients with IBD on immunosuppressive treatment (24 Crohn's disease / 12 ulcerative colitis; 13 male / 23 female, mean ages: 40 years, mean disease duration: 13 years.) Eleven patients received azathioprine monotherapy, 15 patients received biological monotherapy (infliximab/adalimumab) and 10 patients were on combination therapy. The median value of fecal calprotectin was 300 $\mu$g/g at the time of the flu vaccination and it was 330 $\mu$g/g a month later. This difference was not significant ($p = 0.3657$). No significant deviation was found in the laboratory parameters (erythrocyte sedimentation rate, C-reactive protein, leucocytes, haematocrit, thrombocytes) before and after vaccination. Complications after the vaccination were mild: Four patients had local skin reaction (pain, erythema, itches), 6 patients reported "common cold" like symptoms (nasal discharge, dry coughing, fatigue), 2 patients experienced mild relapse. Only one patient perceived "flu like" symptoms such as fever and arthralgia at the 6$^{th}$ week after the vaccination.
**Conclusion:** In our pilot study flu vaccination proved to be safe and did not increase the activity of IBD in patients with immunosuppressive and/or biological therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1363 SATISFACTION WITH LIFE AND COPING IN CROHN'S DISEASE: A GENDER PERSPECTIVE

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**Introduction:** Satisfaction with Life (SWL) and Strategies for Coping with disease form important psychological resources in chronic diseases, but are not adequately researched in Crohn's disease (CD). Our aim was to measure these resources and determine their inter-relationships in Crohn's disease, while exploring gender differences.
**Aims & Methods:** CD patients (aged 18 years or greater) completed a questionnaire incorporating demography, Patient Harvey-Bradshaw Index (P-HBI), treatments, Satisfaction with Life Scale and Brief Cope Inventory (COPE). COPE was sub-classified as Emotion-focused Coping (EFC), Problem-focused Coping (PFC) and Dysfunctional Coping (DYS). We used univariate analysis to compare demographics, disease severity, SWL, and coping strategies between genders, and multiple linear regression analysis to construct gender-specific predictor models of SWL.
**Results:** The cohort comprised 402 subjects; men 39.3% and women 60.1%, respective mean ages $36.5 \pm 12.6$ and $40.1 \pm 14.7$ years ($p = .02$), and P-HBI 4.75 and 5.74 ($p = .01$). Economic status, smoking status, medical treatments and hospitalizations did not differ between genders, but men had more surgeries than women (43% vs. 29.5%, $p = .005$). Men and women had similar SWL scores, 22.27 and 22.38. Men and women had similar scores for EFC, $24.61 \pm 5.63$ and $23.66 \pm 5.65$. PFC was used more by women than men, $16.54 \pm 4.61$ vs. $15.02 \pm 4.56$ ($p = .003$). DYS was used more by women than men, $22.62 \pm 5.24$ vs. $21.04 \pm 6.12$ ($p = .002$). P-HBI was correlated significantly with DYS in men (Pearson correlation coefficient .230) and women (.172). SWL was correlated negatively with P-HBI in men (-.281) and women (-.241). SWL was correlated with EFC in women (.246), and with PFC in men (.246). SWL was negatively correlated with DYS in men (-.364) and women (-.214). PFC correlated with EFC, and DYS with EFC and with PFC, in both genders. SWL was correlated positively with economic status in men (.493) and women (.396). Disease duration, patient age and education were not correlated with SWL. When patients were stratified by disease remission (P-HBI) vs. active disease, the significant differences between men and women with respect to PFC and DYS were confined to the patients in remission. Economic status was the principal predictor of SWL in models constructed separately for men (32.6% of explained variance, model adjusted R square = 0.411) and women (15.2%, 0.335) (both $p < 0.001$).
**Conclusion:** SWL in the CD cohort was only moderate, and associated with economic status but also medical and COPE variables. Women used more dysfunctional and problem-focused coping than men, but with active disease these differences were no longer evident. Physician awareness of these attributes may improve patient care.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1364 PREGNANCY DOES NOT AFFECT FAECAL CALPROTECTIN CONCENTRATION IN HEALTHY PREGNANT WOMEN

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**Introduction:** Fecal calprotectin (CP) is a promising activity marker in the differentiation of inflammatory bowel diseases (IBD) vs. functional gastrointestinal diseases. Non-invasive activity markers are extremely important in conditions, like pregnancy, when endoscopy is not recommended to be performed. Few data is available on the alteration of fecal CP concentration during pregnancy.
**Aims & Methods:** The aim of this prospective study was to determine fecal CP concentrations in healthy non-pregnant and pregnant women and in patients with IBD. Healthy women, pregnant women and patients with active and inactive IBD were prospectively enrolled in the study. Demographic and clinical parameters, clinical disease activity scores in case of patients with IBD were recorded. Blood and stool samples were obtained from every patient to determine C-reactive protein (CRP) and fecal CP levels. Fecal CP concentration was quantified by use of enzyme-linked immunosorbent assay.
**Results:** One hundred and thirty-five subjects were enrolled in the study (24 healthy women, 48 healthy pregnant females, 40 patients with active and 23 patients with inactive IBD). Between subjects with IBD (mean: 788 $\mu$g/g, SD: 1215 $\mu$g/g) and without IBD (mean: 36 $\mu$g/g, SD: 23 $\mu$g/g) was shown significant difference regarding to FC ($p < 0.001$). Mean fecal CP and CRP levels were 36.9 $\mu$g/g (SD: 20.4 $\mu$g/g) and 5.53 mg/l (SD: 4.1 mg/l) in pregnant women. FC was significantly higher in active IBD compared to pregnant ($p < 0.001$) and non-pregnant healthy women ($p < 0.001$). No difference could be detected in the fecal CP concentrations between pregnant and non-pregnant healthy women.
**Conclusion:** Since fecal CP levels did not change during pregnancy, it seems to be useful noninvasive diagnostic tool in pregnancy and maybe beneficial in the future for monitoring disease activity in pregnant patients suffering from IBD. Further studies are necessary to confirm these results.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1365 CLINICAL PREDICTORS OF INTESTINAL BOWEL DAMAGE AND DAMAGE PPROGRESSION ASSESSED BY THE LÉMANN INDEX IN PATIENTS WITH CROHN'S DISEASE

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**Introduction:** Crohn's Disease (CD) frequently shows a gradual progression, leading to accumulation of structural bowel damage (BD), loss of function and disability. The Lémann Index (LI) is an instrument developed to assess the cumulative BD according to stricturing or penetrating lesions detected at endoscopic and radiological evaluation as well as history of surgical resections [1].
**Aims & Methods:** The aim of this study was to evaluate BD progression by LI scoring in patients with CD, in the attempt to identify factors likely to predict its changes. We retrospectively evaluated all consecutive patients with a diagnosis of CD who received 2 or more serial CT or MR enterographies at at least a 6 months time-distance from 2010 to 2015 at our Hospital. Two gastroenterologists and two radiologists reviewed patients' history, endoscopic examinations and cross-sectional images respectively. Two serial LI evaluations were calculated for each patient and matched with CRP levels, Clinical Disease Activity Index

(CDAI), disease location, disease behavior, medical treatments, CD-related hospitalizations and surgeries using the Spearman correlation, the Wilcoxon or the Mann-Whitney tests, as appropriate.
**Results:** Twenty-eight patients were enrolled (15 men, median age 40.3 years). Most of them had a small-bowel (39%) or ileo-colonic (46%) involvement and a luminal (36%) or a stricturing behavior (43%) at baseline. The median LI was 7.7 (interquartile range [IQR] = 2.7–17.9) at baseline and 9.1 (IQR = 4.1–17.7) after a median of 20.7 months (IQR = 10–27.5). History of surgical resections ($P < 0.0001$), stricturing or penetrating behaviors ($P = 0.0041$) and a disease duration $\geq 10$ years ($P < 0.0001$) were predictive of higher LI value at first evaluation. At follow-up, LI increased in 13, remained unchanged in 9 and decreased in 6 patients. LI was more likely to increase in colonic locations (median delta LI 2.5 versus 0.0; $P = 0.34$) and in patients with a disease duration $< 10$ years (median delta LI 0.625 versus 0.0; $P = 0.059$). LI's progression showed no correlation with CRP levels and CDAI. Anti-TNF$\alpha$ treatments were associated with higher LIs at baseline (median LI 25.5 vs 6.3, $P = 0.0175$), and no improvement at the follow-up evaluation (Delta LI 0.6 vs 0.0; $P = 0.0872$).
**Conclusion:** This study confirms that surgical history, complicated disorders or long duration are independent predictors of BD. These data suggest for the first time that patients with colonic locations or with a recent diagnosis of CD have an increased risk of BD progression, thus suggesting that early therapeutic intervention should be taken into account to reduce damage progression. Further studies should now focus on the possible impact of assessing LI in the evaluation of standard and experimental therapeutic strategies.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1366 A PILOT STUDY ASSESSING AGREEMENT AMONG NURSE AND GASTROENTEROLOGIST IN COMPUTING IBD-CLINICAL SCORES

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**Introduction:** Optimal patient care in life-long Inflammatory Bowel Diseases (IBD) benefits from the action of a multidisciplinary team. IBD-nurse can help with assessment and management of patients in remission or with active disease.
**Aims & Methods:** We evaluate the concordance between IBD-nurse and physician in computing Clinical Activity Scores in IBD-patients treated with biologics. From July to September 2015 we enrolled all consecutive IBD-patients treated with biologics at our Unit. For each patient a gastroenterologist and a nurse blindly filled-out a form to assess Harvey-Bradshaw Index (HBI) in Crohn's Disease (CD) or partial MAYO score in Ulcerative Colitis (UC). Each index enable to categorize each patient in one among four classes (remission, mild activity, moderate activity, severe activity). All data were recorded in an electronic database to assess beyond chance agreement (concordance) by k statistic.
**Results:** Eighty-seven patients were enrolled (male 45%, female 55%, CD 61%, UC 39%, infliximab 80%, adalimumab 20%). The agreement in all IBD patients by k value was good (66%), ranging from moderate to substantial (95% CI from 51 to 80%). The main reason of disagreement was about scoring of remission versus mild activity and mild activity versus moderate activity, both in CD and UC patients. The prevalence of severe disease activity was too low in the sample to lead to reliable analysis. With regard of single items of HBI the best agreement was for well-being in the previous day (k 62%, 95% CI 39 to 84%) and the less for abdominal mass (k 35%, 95% CI < 0 to 71%).
**Conclusion:** Our study shows a moderate strength of agreement among nurse and gastroenterologist in evaluating disease activity of IBD-patients through calculation of scores largely used in clinical practice. Despite known simplicity of score administration, there is a need to improve concordance in order to optimize patient care.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1367 SYSTEMATIC REVIEW WITH META-ANALYSIS: THE EFFECT OF TOBACCO SMOKING ON THE NATURAL HISTORY OF ULCERATIVE COLITIS

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**Introduction:** It is well established that tobacco smokers are less likely to develop UC than non-smokers. However, evidence for the role of tobacco smoking on the clinical course of UC is less definitive, with conflicting evidence as to whether this influences the likelihood of needing surgery, rates of relapse of disease activity, proximal extension of disease location, or the development of pouchitis. Despite this, recent data suggests that up to 40% of patients perceive tobacco smoking to have a beneficial effect on disease outcomes in UC. (1) These patients may continue to smoke, exposing themselves to the harmful effects of tobacco smoke without any tangible benefit in UC outcome. We have therefore conducted a systematic review and meta-analysis to examine the effect of tobacco smoking on the clinical course of UC. If tobacco smoking does lead to a less complicated disease course in UC, then this may provide the impetus for researchers to investigate the components of tobacco that are beneficial in UC. However, if there is no effect of tobacco smoking on the natural history of UC, then healthcare professionals can be confident in encouraging smoking cessation in patients with UC, due to the multiple other health benefits provided by quitting smoking.
**Aims & Methods:** To conduct a systematic review and meta-analysis of the effects of tobacco smoking on the natural history of UC A search of MEDLINE, EMBASE and EMBASE classic was carried out (up to December 2015) to identify observational studies reporting data on smoking and rates of colectomy, flare of disease activity, proximal disease extension, and development of pouchitis following panproctocolectomy and ileal pouch-anal anastomosis in patients with UC. Dichotomous data were pooled to obtain odds ratios (ORs), with 95% confidence intervals (CIs).
**Results:** The search identified 16 eligible studies: five (2615 patients) studying colectomy; four (620 patients) reporting on flare of disease activity; four (687 patients) examining proximal disease extension; and three (355 patients) assessing development of pouchitis. Compared with non-smokers, the odds ratio (OR) of colectomy (OR = 0.89; 95% confidence interval (CI) 0.62–1.26), flare of disease activity (OR = 1.26; 95% CI 0.65–2.44), proximal extension of disease (OR = 0.57; 95% CI 0.20–1.66), or the development of pouchitis (OR = 0.57; 95% CI 0.21–1.53) were not significantly lower in smokers.
**Conclusion:** This systematic review and meta-analysis has demonstrated that tobacco smoking, when compared with non-smoking, does not appear to have any effect on colectomy rates in UC. Furthermore, smoking was not associated with any reduction in the rates of flare of disease activity, proximal disease extension, or the development of pouchitis. Given the high morbidity and mortality associated with smoking, and the high proportion of patients who may, falsely, perceive a benefit of smoking on disease outcomes in UC, these data reinforce the need for smoking cessation advice to be provided to all patients with IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1368 USEFULNESS OF CONSECUTIVE FECAL CALPROTECTIN MEASUREMENTS TO PREDICT RELAPSE IN INFLAMMATORY BOWEL DISEASE PATIENTS UNDER MAINTENANCE TREATMENT WITH ANTI-TNF DRUGS

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**Introduction:** Monitoring inflammatory bowel disease (EII) patients with fecal calprotectin (FC) could be useful to predict relapse in clinical practice. Few studies have examined the changes in FC levels during treatment.
**Aims & Methods:** The aim of the study was to evaluate the predictive value of a rapid test of FC to predict flares in IBD patients under maintenance treatment with anti-TNF drugs.
**Methods:** A prospective, observational cohort study was designed. Inclusion criteria were IBD patients in clinical remission for at least six months under a continuous standard dose of 40 mg/eow adalimumab therapy or 5 mg/kg infliximab therapy. Fresh FC was measured using a rapid test (Quantum blue®). FC levels were measured at 4-month intervals for sixteen months. Serum C-reactive protein, erythrocyte sedimentation rate and platelet counts were evaluated in all patients on the same day of faecal sample collection for FC quantification. Relapse was defined as a Harvey–Bradshaw score > 4 in Crohn's disease and a partial Mayo score > 3 in ulcerative colitis. The receiver-operating characteristic (ROC) curve was drawn for diagnostic-accuracy analysis. The optimal cut-off point was that providing the highest sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR +) and negative likelihood ratio (LR-).
**Results:** One hundred and six patients were included (median age 44 years, 51% female), 75% with CD and 25% with UC. After sixteen months of follow-up, 68.4% patients remained in clinical remission whereas the disease relapsed in 31.6% of the patients. FC concentration was significantly higher in those patients who relapsed during the follow-up (477 µg/g, range 131–1800) than in those who maintained in remission (65 µg/g, range 30–880) ($p < 0.001$). The optimal cut-off of fecal calprotectin to predict remission was 130 µg/g according to the ROC analysis. Sensitivity, specificity, positive and negative predictive value of FC to predict relapse were 100%, 80%, 62% and 100%, respectively. FC concentration higher than 300 µg/g resulted in a sensitivity of

66.7%, specificity of 93.8%, positive predictive value (PPV) of 78.3% and negative predictive value (NPV) of 89.4%. The positive likelihood ratio (LR+) is 10.8. Two consecutive FC measurements > 300 µg/g were identified as the best predictor for flare with a PPV of 86%, NPV of 72.7% and LR + 12.9. According to ROC analysis, FC was significantly better to predict relapse than C-reactive protein or erythrocyte sedimentation rate.
**Conclusion:** In IBD patients under anti-TNF therapy, FC is useful to monitor patients for relapse. FC levels lower than 130 µg/g exclude relapse over at least the following four months with a negative predictive value of 100%. FC levels higher than 300 µg/g predict relapse within the following four months with a positive predictive value (PPV) of 78.3%. Two consecutive FC measurements higher than 300 µg/g are the best predictors of flare with a PPV of 86%.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1369 DEVELOPMENT AND VALIDATION OF A DEVICE FOR RAPID MONITORING OF ADALIMUMAB IN SERUM OF INFLAMMATORY BOWEL DISEASE PATIENTS

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**Introduction:** Therapeutic drug monitoring of adalimumab is recommended to improve therapeutic outcomes in patients with inflammatory bowel disease. To do this, we previously developed the MA-ADM28B8/MA-ADM40D8 ELISA to measure adalimumab serum concentrations and showed an equal performance of this ELISA compared to TNF-coated adalimumab assays[1]. The disadvantages of ELISA are the rather long time-to-result and the necessity of collecting multiple samples in order to decrease the price per adalimumab determination. Recently, a fiber-optical surface plasmon resonance (FO-SPR)-based sensor was combined with gold nanoparticles to measure infliximab in serum[2].
**Aims & Methods:** To develop and validate an assay for measuring a single adalimumab serum sample within 45 minutes. Similar to ELISA, the capture antibody MA-ADM28B8, was immobilized on a gold-sputtered fiber surface; and the detection antibody MA-ADM40D8 was conjugated to gold nanoparticles to amplify the detection signal. Different concentrations of adalimumab were spiked in buffer and serum diluted 1/400 with the same buffer. Here, a calibration curve was measured using one FO probe which was regenerated between each sample. Infliximab was applied to test the assay's specificity. Performance of the FO-SPR sensor was compared with ELISA using six serum samples of adalimumab-treated patients.
**Results:** A dose-response curve ranging from 2.5 – 40 ng/ml was obtained in buffer and 1/400 diluted serum, allowing quantification of 1 to 16 µg/ml adalimumab in serum. Non-specific infliximab concentrations up to 16 µg/ml showed no significant signals. Using a pre-functionalized fiber, the sensor requires less than 45 min for measuring a single adalimumab serum sample. Comparison of measurements between FO-SPR and ELISA revealed excellent correlation (Pearson r coefficient of 0.994 and intraclass coefficient of 0.993).
**Conclusion:** A rapid bioassay using the FO-SPR platform was established and revealed excellent correlation with ELISA. The reduced assay time and the possibility of measuring a single sample are major advantages compared to ELISA. Considering its full automation and miniaturization, it would be a valuable point-of-care diagnostic tool for adalimumab measurements.
**Disclosure of Interest:** S. Vermeire: Financial support from MSD and Abbvie, lecture fees from MSD, Abbvie, Takeda, Falkand Tillotts, consultancy fees from MSD, Abbvie, Takeda, Falk, Ferring, Shire, Galapagos, Hospira, Mundipharma, Genetech/Roche, Pfizer and Celgene.
A. Gils: Lecture fee (s): MSD, Janssen Biologicals, Abbvie, Pfizer, Takeda; Consultancy: UCB. Conflict with: license of infliximab, anti-infliximab and adalimumab ELISA from Institution to apDia and with lateral flow infliximab to R-Biopharm AG.
All other authors have declared no conflicts of interest.

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## P1370 PHENOTYPE CORRELATION IN INFLAMMATORY BOWEL DISEASE (IBD) COMPARED TO SEROLOGIC ANTIBODY ACTIVITY AT DIAGNOSIS AND AFTER TREATMENT

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**Introduction:** Serologic nuclear and antimicrobial antibodies have been proposed as predictive markers of disease course and complications in inflammatory bowel disease (IBD), however their stability over time have been questioned.
**Aims & Methods:** The aim of the study was to compare antibody titres before and after treatment in newly diagnosed adult IBD patients with regard to gender, age, disease distribution and grade of inflammation. Patients were included as a part of a prospective population based study (IBSEN II). All diagnoses were revised at follow up. Selected antibodies (ASCA IgA, ASCA IgG, Anti-OmpC IgA, Anti-CBir1 IgG, Anti-I2 and pANCA) (Prometheus laboratories Inc., San Diego) were evaluated at inclusion and follow-up within 2 years. C-reactive protein (CRP) and fecal calprotectin were used as markers for inflammation.
**Results:** In total 221 patients were included. Initially 60 patients were diagnosed as ulcerative colitis (UC), 36 as Crohns disease (CD), 8 as IBD-U, 7 as possible IBD and 110 as non-IBD (controls). All patients, except non-IBD, were invited to follow-up with re-examination within 2 years and 89 accepted. At follow-up 17 patients did not have data on antibodies, reducing the numbers for paired comparison to 36 (UC) and 21 (CD). **Reference values:** (EU/ml, ELISA) for antibodies were: ASCA IgA < 8.5, ASCA IgG < 17.8, Anti-OmpC IgA < 10.9, Anti-CBir1 IgG < 78.4, Anti-I2 < 368, and for pANCA detected (positive) or not detected. UC patients 75% (27/36) was pANCA-positive at diagnosis and 64% (23/36) patients did not change their status at follow-up while 36% (13/36) did. The percentages of positive values of the other antibodies were as follows: Anti-I2 (53%), Anti-OmpC (6%), ASCA IgA (25%), ASCA IgG (3%), and Anti-CBir1 (8%). Additionally they had not changed significantly at follow-up. CD patients ASCA IgA was positive in 38% (8/21) and 43% (9/21) at diagnosis and follow-up, respectively. 24% (5/21) changed their status. pANCA was positive in 48% (10/21) and 33% (7/21) at diagnosis and follow-up, respectively. 33% (7/21) changed their status. Anti-I2 was positive in 71% (15/21) and 67% (14/21) at diagnosis and follow-up, respectively. 14% (3/21) changed their status. Positive values in the remaining antibodies at diagnosis: Anti-OmpC (0%), ASCA IgG (24%, 5/21), and Anti-CBir1 (19%, 4/21). Moreover, no significant changes occurred at follow-up. Phenotype: There were no statistically significant associations between positive serological biomarkers and grade of inflammation, gender and age, nor disease distribution in the IBD study sample. (all $p > 0.60$)
**Conclusion:** Our results suggest that pANCA and ASCA are not stable in IBD patients, in contrast to previous studies. An explanation could be that children are excluded in our study and that there are differences between adults and children with regard to antibody stability. Further, there were no statistical associations between positive serological biomarker (s) as tested and disease phenotype nor gender and age. Our results do not support the use of serological biomarkers as diagnostic nor prognostic tools in an adult clinical practice as a routine practice, however our findings are based on small numbers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1371 ACQUIRED VON WILLEBRAND SYNDROME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Acquired von Willebrand syndrome (AvWS) is observed in numerous diseases, including immunological and cardiovascular disorders, malignancies, myeloproliferative disorders, infections. It can occur as well as a side-effect of some medications. Bleeding from gastrointestinal tract is one of the most important clinical symptoms of AvWS. The diagnosis of the AvWS type 2a is based on the same criteria as the diagnosis of von Willebrand disease type 2 – the ratio of ristocetin cofactor activity (vWF:RCo) to vWF antigen concentration (vWF:Ag) (vWF:RCo/vWF:Ag) or vWF collagen binding test (vWF:CB) to vWF:Ag (vWF:CB/vWF:Ag) should be less than 0.7.
**Aims & Methods:** The study aimed to assess the risk of AvWS occurrence in patients with inflammatory bowel disease (IBD). 85 patients with IBD, including 47 patients with ulcerative colitis (UC) and 38 with Crohn's disease (CD) as well 50 healthy volunteers were involved in the study. In all the patients disease activity, localization of inflammatory changes and presence of complications has been assessed. vWF:Ag, vWF:RCo, vWF:CB, leucocytes, platelets, C reactive protein (CRP), fibrinogen, albumin, haematocrit were measured in all subjects. The ratio of vWF:RCo/vW:FAg and vWF:CB/vWFAg as well the odds

ratio (OR) of vWF:RCo/vWF:Ag or vWF:CB/vWF:Ag less than 0.7 in comparison to the control group was calculated.
**Results:** Plasma vWF:Ag was higher in CD and UC patients than in controls (for both $p < 0.0001$). Additionally, in the IBD group approximately 50% of patients had vWF:Ag higher than 150%, whereas in the control group only 8%. In the UC group the OR of vWF:Ag higher than 150% was 8.7 (95%CI: 2.7–28.1), and in the CD group - 16.2 (95%CI:4.8–54.0) in comparison to the control group. vWF:CB was lower in the UC group in comparison with both CD as well the control group. Such differences were not observed for vWF:RCo. In IBD group there was 13 patients with vWF:RCo/vWF:Ag < 0.7, whereas in the control group there was not any. In UC group OR for vWF:RCo/vWF:Ag < 0.7 was 18.7 (95%CI: 1.0–337.4) in comparison to the control group and in CD group - 20.2 (95%CI: 1.1–370.8). In UC group OR for vWF:CB/vWF:Ag < 0.7 was 11.9 (95%CI: 4.4–32.4) and in CD group 13.3 (95%CI: 4.6–38.1) in comparison to the control group.
**Conclusion:** This is the first study to show that in UC and CD patients there is an increased risk of AvWS occurrence. In spite of tendency to hypercoagulability in IBD patients, in some cases an increased risk of bleeding might be observed. However, research involving a larger number of patients is required to confirm this observation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1372 7-ALPHA-CHOLESTENONE AND FAECAL CALPROTECTIN IN PATIENTS WITH COLLAGENOUS COLITIS

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**Introduction:** Collagenous colitis (CC) causes chronic, watery diarrhoea [1]. Bile acid malabsorption (BAM) often accompanies CC [2,3] and CC can respond to treatment with bile acid sequestrants [4]. The European Microscopic Colitis Group (EMCG) advises that BAM should be sought in investigation for CC [1]. The selenium-labelled homocholic acid taurine (SeHCAT) test is considered the gold standard for BAM diagnosis; however, serum 7-alpha-hydroxy-4-cholesten-3-one (7aC) is simpler and less expensive, with comparable sensitivity [5]. Faecal calprotectin (FC) is well established as a biomarker of bowel inflammation, but data on CC is scant [6]. We present data from a tertiary referral centre on 7aC and FC in patients with CC.
**Aims & Methods:** Pathology records were interrogated for patients diagnosed with CC (2000–2015), extracting results on 7aC and FC. Results are presented as mean (±SD) or median (range).
**Results:** Over 15 years, 399 patients were diagnosed with CC (280 F/119 M). Of these, 164 were excluded from further analysis due to lack of appropriate data. 7aC was available in 83 (20.8%) patients, mean levels of 11.5 ± 9.70 ng/ml. 11/83 (13.3%) patients had elevated 7aC. FC levels were measured in 101 (25.3%) patients, mean levels 251.89 ± 282.62 µg/g. Of these, 76/101 (75.2%) had elevated FC ≥ 50 µg/g (FC ≥ 100 µg/g: 63/101; FC ≥ 200 µg/g: 30/101). Of the 101 patients with FC measurement, 76 had FC results ± 30 days from the point of histological diagnosis. In this group, median FC was 165 µg/g, range 20–1375 µg/g.
**Conclusion:** This is the first cohort data on 7aC in CC. Our findings confirm that a significant proportion of CC patients have co-existing BAM; however, the incidence is lower than that reported in other studies using SeHCAT. The high incidence of raised FC in our cohort supports the position that FC is a useful marker of histologic inflammation in CC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1373 BIOLOGICAL THERAPY IS ABLE TO HALT CROHN'S DISEASE PROGRESSION: A PROSPECTIVE, LONG TERM STUDY USING THE LÉMANN INDEX

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**Introduction:** Crohn's disease (CD) is a chronical and progressive condition. It has been established that even during remission a subclinical inflammation persists. This condition may lead to stricturing or penetrating lesions and at least surgical resection. To date, the Lémann Index (LI), is the only instrument developed and validated to assess structural bowel damage related to disease evolution. This Index was recently applied in a retrospective study to demonstrate that biological therapy was able to halt CD progression.
**Aims & Methods:** The primary aim of our prospective study was to evaluate the capability of biological therapy to halt or decrease LI in a series of consecutive CD patients. The secondary aim was to correlate delta LI to Harvey Brashaw Index (HBI) and PCR values during a long-term follow up period. We prospectively enrolled consecutive CD patients who were starting biological therapy at our IBD center and we followed-up them every 6 months by means of clinical and biochemical evaluation and every year by radiological and endoscopic assessment in order to calculate the LI. Clinical activity was measured according to HBI (remission defined by HBI < 5) and a CRP < 5 mg/L was considered normal.
**Results:** We prospectively enrolled 39 CD patients (26 Male, median age 38 years, range 18–67) with a median follow-up of 19 months (range 6–28 months). Out of them, 24 (61.5%) were on Adalimumab therapy and 15 (48.5%) patients were on Infliximab therapy. Median LI at the beginning of follow-up and every years for the subsequent two years was respectively 4.6 (0.9–29.8), 4.6(0–29.4) and 2.7 (0–26.2) with no significant difference during these years compared to baseline ($P = 0.53$, $P = 0.25$). There was no significant difference in terms of median LI at the beginning [4.7, (0.9–29.8) vs. 3.2 (1.6–26.5), $p = 0.36$] and end [4.6 (0–29.4) vs. 2 (0–26.2), $p = 0.67$] of follow-up between patients with mild disease compared to patients with moderate/severe disease at baseline. Moreover, there was no difference in terms of median LI comparing patients with an increased CRP values (> 5 mg/L) to patients with normal CRP values both at the start [3.8 (0.9–29.8) vs. 5.7 (1.3–26.6), $p = 0.67$] and end [4.6 (0–29.4) vs. 7.3 (0–29.2), $p = 0.66$] of follow-up period.
**Conclusion:** Our data from a prospective cohort study confirm that biological therapy is able to halt disease progression during a long-term follow up. Moreover, we showed that neither CRP values or HBI as measured at the beginning of biological therapy were able to predict the worsening of bowel damage.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1374 DETECTION OF ANTI-INFLIXIMAB ANTIBODIES IS IMPACTED BY ANTIBODY TITER, INFLIXIMAB LEVEL AND IGG4 ANTIBODIES: A SYSTEMATIC COMPARISON OF THREE DIFFERENT ASSAYS

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**Introduction:** There is scant information on the accuracy of different assays used to measure anti-infliximab antibodies (ADAs), especially in the presence of detectable infliximab (IFX).
**Aims & Methods:** We thus aimed to evaluate and compare three different assays for the detection of IFX and ADAs and to clarify the impact of the presence of circulating IFX on the accuracy of the ADA assays. Blood samples from 79 ulcerative colitis (UC) patients treated with IFX were assessed for IFX levels and ADAs using three different assays: an in-house assay and two commercial kits, semi-fluid phase ELISA (SFPE) and Bridging ELISA (BE). Sera samples with ADAs and undetectable levels of IFX were spiked with exogenous IFX and analysed for ADAs.
**Results:** The three assays showed 92–96% agreement for the measured IFX level. However, the in-house assay and SFPE assays detected ADAs in 34 out of 79 samples, whereas BE only detected ADAs in 24 samples. Samples negative for ADAs with BE, but ADA-positive in both the in-house and SFPE assays, were positive for IFX or IgG4 ADAs. In spiking experiments, a low concentration of exogenous IFX (5 µg/mL) hampered ADA detection with BE in sera samples with ADA levels of between 3 µg/mL and 10 µg/mL. In the SFPE assay detection interference was only observed at concentrations of exogenous IFX higher than 30 µg/mL. However, in samples with high levels of ADAs (> 25 µg/mL) interference was only observed at IFX concentrations higher than 100 µg/mL in all three assays. Binary (IFX/ADA) stratification of the results showed that IFX+/ADA- and IFX-/ADA+ were less influenced by the assay results than the double positive (IFX+/ADA+) and double negative (IFX-/ADA-) combination.
**Conclusion:** All three methodologies are equally suitable for measuring IFX levels. However, erroneous therapeutic decisions may occur when patients

show double negative (IFX-/ADAs-) or double positive (IFX+/ADAs+) status, since agreement between assays is significantly lower in these circumstances.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1375 UTILITY OF EMERGENCY DEPARTMENT CT SCANS IN PATIENTS WITH ULCERATIVE COLITIS

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**Introduction:** Although abdominal CT scans are commonly ordered as part of the emergency department (ED) work-up for patients with ulcerative colitis (UC), their utility in management is unclear.
**Aims & Methods:** Our hypothesis is that most ED CT scans have limited diagnostic and therapeutic impact. The aims of our study were to determine the rate and predictors of ED CT scans among patients with UC. In addition, we also sought to identify variables that can predict significantly abnormal findings on EDCT. Methods: UC patients identified from a single-institution IBD database who were evaluated in the ED from 2009–2015 were retrospectively reviewed. Demographic and clinical data including laboratory and radiological investigations were collected. Patients with recent UC diagnosis ( < 3 months), previous colectomy and those with non-GI-related ED visits were excluded. We determined the proportion of patients with a new major CT finding and evaluated clinical and laboratory predictors of relevant diagnoses. Findings of active colitis on EDCT were censored. We used the X-square test and multivariate regression analysis to test the association of the outcomes with variables of interest.
**Results:** Results: During this interval, 365 UC patients presented to the ED. Of these, 261 were excluded (no GI complaint, no established UC, prior colectomy). The remaining 138 patients (51% male) had a total of 260 ED visits (median 1, range 1–16) of which 38.1% resulted in a CT scan (median 1/patient, range 1–8) and 36 (36.4%) had major new findings (intra and extra-intestinal). In univariate analysis, abdominal pain significantly increased (RR = 1.5; CI 1.2–1.7) and rectal bleeding (RR = 0.38, CI 0.2–0.7) and being on any IBD medications (RR = 0.86, CI 0.75–0.98) significantly decreased the likelihood of ordering a CT scan while a plain abdominal X-ray order had a negative trend. 44% of patients had a CT or MRI in the previous year and this did not affect the chance of getting a new EDCT. In univariate analysis, rectal bleeding (RR = 0.14), diarrhea (RR = 0.33), and an elevated CRP (RR = 0.45) were negative predictors of new significant CT findings while there was no interaction with taking any IBD medications. On multivariate analysis, only diarrhea remained a significant negative predictor (RR = 0.19, CI 0.065–0.58). Overall, 67.3% ED visits resulted in hospitalization, a rate which was not affected by ordering a CT or the presence of significant findings.
**Conclusion:** UC patients presenting to the ED frequently undergo CT scans with relatively modest yield. Diarrhea as the main complaint is the only significant negative predictor for major new findings on the abdominal CT scan. Ordering a CT scan or a new major CT diagnosis did not affect the likelihood of hospitalization. A risk stratification score for improving the yield of EDCT could be developed using simple clinical variables.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1376 A CHANGE IN ΔMCV PREDICTS MUCOSAL HEALING IN PATIENTS WITH CROHN'S DISEASE UNDER COMBINATION THERAPY

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**Introduction:** Higher tioguanine (6-TGN) levels have been associated with better clinical and endoscopic outcomes in patients with inflammatory bowel disease under thiopurine therapy. Unfortunately dosing of 6-TGN levels is not available in most centers. Previous studies have suggested that an elevated erythrocyte mean corpuscular volume (MCV) can be a valid surrogate of adequate 6-tgn levels.
**Aims & Methods:** This was a retrospective study using a cohort of patients under combination therapy with Infliximab and azathioprine followed in a single center. We evaluated the influence of a ΔMCV in major endpoints including clinical and endoscopic response and remission at the end of the first year of treatment. Clinical response was defined as a decrease of 3 points in Harvey-Bradshaw Index and clinical remission as a Harvey-Bradshaw Index ≤4. Endoscopic response was defined as improvement in endoscopic appearance and endoscopic remission as the absent of ulcers. In a subgroup of patients anti-TNF pharmacokinetics (serum levels and antibodies) were also evaluated.
**Results:** 143 patients with Crohn's Disease (CD) were included, 67 patients (53.1%) male with mean age of 28 ± 11.5 years. MCV at baseline and at week 48 of treatment was 88.2 fL ± 15.8 and 89.7 fL ± 4.7, respectively. At the end of the first year of combination therapy, 13.3% patients achieved clinical response, 74.1% clinical remission, 40.6% endoscopic response and 43.4% endoscopic remission.
Patients with higher variations in MCV were more likely to be in clinical remission (3.16 ± 4.94 vs -0.95 ± 6.44, p < 0.001). There was no statistical significance between ΔMCV and clinical response.
Patients with endoscopic response and remission had higher ΔMCV (2.57 ± 3.70 vs -3.38 ± 7.05, p < 0.001 and 3.17 ± 3.97 vs -0.27 ± 5.74, p = 0.006, respectively). The area under the receiver-operating curve (auroc) for predicting endoscopic remission, endoscopic response and clinical remission according to the ΔMCV was 0.665(95%CI 0.532–0.797, p = 0.025), 0.714 (95%CI 0.545–0.883 p = 0.011) and 0.711 (95%CI 0.616–0.806, p < 0.001), respectively.
For each unit increase in MCV level there was a significant increase in the probability of achieving clinical remission- OR 1.17 (95%CI 1.07–1.27, p = 0.001), endoscopic response- OR 1.29 (95%CI 1.10–1.50, p = 0.001) and endoscopic remission- OR 1.17 (95%CI 1.027–1.326, p = 0.018). There was a negative correlation between C-reactive protein (CRP) levels and ΔMCV (spearman rho -0.254, p = 0.003); patients with a negative CRP at week 48 had higher ΔMCV (5.67 ± 5.37 vs 3.45 ± 4.71, p = 0.012). We found no significant association between ΔMCV and Infliximab through levels and antibodies.
**Conclusion:** Our results suggest that there is an association between ΔMCV and better outcomes in CD patients under combination therapy. Assessment of ΔMCV may be an alternative to 6-TGN dosing where unavailable
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1377 SERUM NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN IN INFLAMMATORY BOWEL DISEASE: A NEW ACTIVITY MARKER

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**Introduction:** Neutrophil gelatinase-associated lipocalin (NGAL) is a bacteriostatic protein with pro-inflammatory effect. Furthermore, this protein is overexpressed in patients with inflammatory bowel disease.
**Aims & Methods:** Our aim was determine the relationship between serum NGAL levels, type of inflammatory bowel disease and inflammatory activity. Methods: 17 IBD patients with inflammatory activity and indication of anti-TNF treatment were collected (average age 46 years, 60% women). 3 patients were diagnosed by ulcerative colitis and 14 Crohn's disease. Serum NGAL determination was measured by immunoassays (ELISA) at baseline, post-induction (8 weeks) and 6 months after the initiation of anti-TNF. Regarding the type of anti-TNF treatment, 7 patients received infliximab and 10 adalimumab. Clinical activity index (Harvey-Brandshaw and Mayo Index) and biological markers (RCP, ESR, platelets, leukocytes and hemoglobin) were collected.
**Results:** A decreased of NGAL at 6-month post-treatment was observed in patients who obtained clinical response (n = 10) (20.48 ± 9.33 vs 16.93 ± 4.33 ng/ml; p = ns). However, an increase in NGAL levels was obtained at 6-month treatment in patients without clinical response (n = 7) (21.07 ± 13.36 vs 30.75 ± 19.47 ng/ml; p = 0.043) There was a positive correlation between clinical index and serum NGAL levels at baseline r: 0.52, p = 0.036 and at 6-month after initiation of anti-TNF r: 0.70, p = 0.002. A correlation between serum NGAL levels and biological parameters were observed such as RCP r: 0.61, p = 0.012, platelets r: 0.68, p = 0.004, leukocytes r: 0.72, p = 0.001 and ESR r: 0.56, p = 0.023 at week 8 post-treatment. After 6 months, there was still a positive correlation between NGAL and RCP r:0.70, p = 0.002, platelets r: 0.56, and leukocytes r:0.72, p = 0.001. No correlation was observed between NGAL and hemoglobin.
**Conclusion:** Serum determination of NGAL is useful as biomarker in inflammatory activity in IBD. Serum NGAL is increased in active IBD. A positive correlation is observed between NGAL and other markers of inflammation demonstrating its role in pathophisiology of IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1378 BOWEL DAMAGE IN CROHN'S DISEASE: DIRECT COMPARISON OF ULTRASONOGRAPHY- AND MAGNETIC RESONANCE-BASED LEMANN INDEX

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**Introduction:** Recently, the Lémann Index (LI) was developed to assess bowel damage (BD) in Crohn's disease (CD). LI should be evaluated by using magnetic resonance (MR) or CT-enterography in association with endoscopy.
**Aims & Methods:** Our aim was to investigate the concordance between ultrasonography-based LI (US-LI) and MR-based LI (MR-LI). We retrospectively evaluated all consecutive CD patients referred to our IBD Unit from February to September 2015. All patients had undergone ileo-colonoscopy, US and MR within 1 month. The US/MR diagnosis of CD and the assessment of extension/complications were performed in accordance with the current literature. US-LI and MR-LI were calculated for each patient by scoring: previous surgery, location, extension, intestinal complications. Furthermore, we evaluated the association between LI and: CD duration (months) and Harvey-Bradshaw index (HBI) and other relevant clinical features. Furthermore, in accordance with recent literature a LI > 4.8 was considered indicative of BD. Statistical analysis included T-student, ANOVA, chi-square, Cohen's k coefficient and Spearman's r test. All differences were considered significant when $p < 0.05$.
**Results:** Finally, 30 CD patients were enrolled. Regarding CD location, 36% showed ileal disease (L1), 10% had an isolated colonic CD (L2) while 64% had an ileo-colonic disease (L3). Moreover, 20% of patients presented a non-complicated behavior (B1); 47% had almost one stricture (B2) while the remaining 33% showed a penetrating CD (B3). Perianal CD was observed in 23% of subjects, while 43% had undergone previous surgery. Mean HBI was 12.7 + 6. When calculating BD, mean US-LI and MR-LI were 6.44 (95%CI 3.6–9.2) and 6.9 (95%CI 4.2–9.7), respectively ($k = 0.90$; $p < 0.001$), with 16 patients (53%) showing a LI indicative of underlying BD. No significant correlation was evident between LI and HBI ($p = 0.9$) while a significant correlation was found between both US-LI and RM-LI and CD duration ($p = 0.01$).
**Conclusion:** US-LI shows high concordance with MR-LI and could be considered a good option for assessing BD in CD by using a high available and relatively inexpensive procedure. Our data confirm the low accuracy of the current clinical activity indices in assessing BD in CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1379 PATIENT-NEAR INFLIXIMAB TROUGH-LEVEL TESTING BY A NOVEL QUANTITATIVE RAPID TEST: THE QUANTUM BLUE INFLIXIMAB ASSAY

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**Introduction:** Therapeutic drug monitoring (TDM) has become standard clinical practice over the last few years. There is overwhelming clinical evidence that optimization of anti-TNF drugs improve clinical outcome partly because this decreases the risk for anti-drug-antibodies (ADA) and improves the efficacy of the drug itself. There is also another aspect for advocating TDM, that is improving the health economic aspect of these very expensive drugs. Approximately 44% of the patients (pts) are correctly dosed, 21% under dosed and 26% had IFX levels above 7, i.e. had unnnecessary high levels. Consequently, nearly half of the pts need a dose optimization. However, this has been hampered by the absence to near patient test which could deliver trough level information within the time frame of a hospital consultation. Currently, tests are mainly ELISA based, performed in a centralized laboratory facility and the test result is usually delayed for several days. This means that when the patients comes for infusion, the trough level is not available for dose adjustment until next infusion time, often weeks away.
**Aims & Methods:** Objective of the study: The study had two aspects; first is to correlate a CE-marked rapid test for IFX trough level, the Quantum Blue Infliximab test (QB-IFX®) (Bühlmann Laboratories, Basel, Switzerland) to an ELISA assay in routine use at the Norwegian Radium Hospital. Secondly, to correlate the performance of such a test done by; A) a nurse and B) a trained laboratory person. Methods and materials: The study comprised 19 pts with IBD receiving IFX treatment (Remicade or Remzina). At the day of infusion, ordinary routine bloodtest (CRP, Hb, LFT etc) and plasma for IFX-trough ELISA was collected in addition to 3 ml serum for QB-IFX rapid test. Part A: A nurse (IS) received one hour of "laboratory" training before running the QB-IFX under supervision of AR. The serum was thawed, vortexed and diluted 10uL in 190 uL assay buffer and again vortexed for 5 sec. 70uL was applied to the rapid test cassette and a 15 min. timer started. A new cassette was loaded every two min. After 15 min, the first cassette was read using the "Q B- IFX®" dedicated electronic reader. Subsequently, a cassette was read every two min thereafter. Part B: The same procedure was followed but this time by a highly experienced lab technician (GHM).
**Results:** The Pearson's r between the QB-IFX and the ELISA was 0.94, $p < 0.0001$. Passing- Bablok analysis resulted in a slope of 1 (0.73–1.17, 95% CI) and a bias (Bland -Altman) of -11%. Furthermore, the Pearson's r between the QB-IFX values done by a nurse and a lab technician was 0.92, $p < 0.0001$.
**Conclusion:** Conclusion: To our knowledge, this is the first study that documents a close correlation between an ELISA test and a 15 min. rapid test for IFX trough level. Furthermore, we have shown that such a test can accurately be performed by a nurse at a point-of-care site, e.g. an infusion centre. The results implies that TDM now can be moved from a distant laboratory to a near pts facility like an infusion centre and ensure correct dosing and instant decision making in IBD as well as in other pts receiving IFX treatment.
**Disclosure of Interest:** A. Røseth: I am affiliated part time with Buhlmann Laboratories as a medical advisor. Otherwise, Im full time employed at Lovisenberg Hospital Oslo
All other authors have declared no conflicts of interest.

## P1380 HOME MONITORING OF DISEASE ACTIVITY AND FECAL CALPROCTIN IN ADULT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Due to the chronic relapsing nature of Inflammatory bowel disease (IBD) it is of great importance to detect and treat a relapse as soon as possible in order to decrease the total inflammation burden, decrease or postpone the risk of surgery and possibly change of disease course. A validated Fecal Calprotectin (FC) home testing kit and smart phone application (app) has been added to an existing eHealth web app, thereby making it possible for the patients to monitor their disease activity using clinical scores and FC from home. FC levels can be obtained within 18 minutes using the home testing kit and is shown on the smart phone. Results from clinical scores and FC are categorized in a traffic light manner on the eHealth web app for instant recommendation of individualized treatment strategy – treat to target[1].
**Aims & Methods:** Our aim, with this one-year randomized control trail of 120 adult IBD patients, is to determine if an eHealth screening procedure for disease activity should be implemented in clinical practice 'on demand' or 'every 3 months'. Both groups use the web program noh.constant-care.dk to tightly monitor their disease activity either 'on demand' or 'every 3 months'. The web algorithm consists of a short disease questionnaire either Harvey-Bradshaw Index (HBI) for Crohn's disease (CD) or Simple Clinical Colitis Activity Index (SCCAI) for Ulcerative colitis (UC) plus home monitoring of FC, which together gives a total inflammation burden scoring (TIBS). Moreover, but not a part of the TIBS disease activity web algorithm, patients also enter in the web program their fatigue score (FACIT-F), Medication Adherence Report scale (MARS), Quality of Life (s-IBDQ) and Copenhagen IBD Disease Course (CIDC) type. The latter will only be measured at inclusion and at follow up.
**Results:** So far, baseline results of ninety-eight IBD patients are available, 78 with UC and 20 with CD. All of them have fulfilled HBI or SCCAI on the web program at inclusion. Ninety (91.8%) FC results were obtained at baseline and eight (8.2%) were missing. According to the web algorithm, patients were in median in remission in both groups, 'every 3 months' vs. 'on demand', Median (interquartile range): FC in mg/kg 70 (20–560) vs. 88 (20–808), SCCAI: 1 (0–3) vs. 1 (0.5–2.5), HBI 1 (0–2) vs. 3 (1–6) and TIBS 5.5 (0–33) vs. 9 (2–34). Baseline descriptive data for the ninety-eight patients randomized to 'on demand' or 'every 3 months' is listed in table 1 and no significant differences between the two groups were found.
**Conclusion:** Adult IBD patients in remission regarding disease activity were included. Feasibility and usability of the web apps were acceptable and only 8.2% failed home monitoring FC test at inclusion, mostly due to technical problems prior to the app being CE-marked and distributed from App Store and Play Store. Results are awaiting for long-term course.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1381 ENDOSCOPY WITH LINKED COLOR IMAGING AND NARROW BAND IMAGING EFFICIENCY FOR EVALUATION OF MUCOSAL HEALING IN PATIENTS WITH QUIESCENT ULCERATIVE COLITIS

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**Introduction:** Endoscopic determination of mucosal healing is important for the prognosis of ulcerative colitis (UC) recurrence in clinical remission because many cases often remain in the active phase endoscopically. We previously reported that the classification based on magnifying chromoendoscopy (MD, MI, and MR; *Inflamm Bowel Dis* 15: 2009) reflects the histological condition of the mucosa in quiescent UC. In the present study, we classified Linked Color

**P1380 Table 1:** Baseline characteristics of patients

| | Every 3 Months | On Demand | p |
|---|---|---|---|
| Male/Female, number (%) | 19(38.8)/30(61.2) | 23(46.9)/26(53.1) | 0.42 |
| Age (yr), median (IQR) | 45(33–53) | 48(33–62) | 0.53 |
| IBD diagnosis, number (%) Ulcerative colitis (UC) Crohn's disease (CD) | 42 (85.7) 7 (14.3) | 36 (73.5) 13 (26.5) | 0.14 |
| Prior Surgery, number (%) | 4 (8.2) | 5 (10.2) | 0.73 |
| UC extent, number (%) E1, proctitis E2, left side E3, extensive | 18 (42.9) 8 (19.0) 16 (38.1) | 16 (44.4) 8 (22.2) 16 (33.3) | 0.23 |
| CD location, number (%) L1, small bowel L2, colonic L3, ilea-colonic | 0 3 (42.9) 4 (57.1) | 1 (7.7) 4 (30.7) 8 (61.5) | |
| CD behaviour, number (%) B1, Inflammatory B2, stricturing B3, penetrating | 6 (85.7) 1 (14.3) 0 | 8 (61.5) 1 (38.5) 0 | |
| IBD duration (yr), median (IQR) | 12 (6–19) | 7 (4–15) | 0.11 |
| UC disease activity (SCCAI), median (IQR) | 1 (0–3) | 1 (0.5–2.5) | 0.37 |
| CD disease activity (HBI), median (IQR) | 1 (0–2) | 3 (1–6) | 0.17 |
| Fecal calprotectin mg/kg, median (IQR) | 70 (20–560) | 88 (20–808) | 0.88 |
| Total inflammation burden scoring (TIBS), median (IQR) | 5 (0–33) | 9 (2–34) | 0.26 |
| Short-IBD-quality of life, median (IQR) | 60 (49–65) | 56 (49.5–62.5) | 0.09 |
| Medication adherence (MARS), median (IQR) | 117.5 (25–124) | 121 (112–125) | 0.17 |
| Fatigue Score (FACIT), median (IQR) | 12 (9–16) | 13 (9.5–20) | 0.49 |
| Copenhagen IBD Disease Course type, number (%) A: Mild IBD with indolent course B: Mild IBD with aggressive course C:Chronic IBD with continous course D: Chronic IBD with intermittent course | 20 (44.4) 5 (11.1) 4 (8.9) 16 (35.6) | 27 (57.5) 2 (4.3) 5 (10.6) 13 (27.7) | 0.44 |
| Medication, number (%) 5-ASA Biologicals Immunosuppressants Combination treatment No treatment | 24 (49.0) 6 (12.2) 1 (2.0) 10 (20.4) 8 (16.3) | 26 (53.1) 2 (4.1) 2 (4.1) 12 (24.5) 7 (14.3) | 0.61 |
| Smoking, number (%) Current Former Never | 4 (8.5) 13 (27.7) 30 (63.8) | 5 (10.6) 15 (31.9) 27 (57.4) | 0.41 |

Imaging (LCI; Fujifilm, Tokyo, Japan) findings of the mucosa and compared these with findings from conventional endoscopy and magnifying chromoendoscopy; furthermore, we compared the extent of mucosal inflammation of biopsied tissues to determine if LCI is suitable to access mucosal healing. LCI is the color enhancement imaging new technology for emphasizing slight color difference on mucosa.

**Aims & Methods:** We performed colonoscopy to assess mucosal healing in UC in clinical remission using the classifications for conventional endoscopy (Mayo endoscopic score 0, 1, 2, and 3) and magnifying chromoendoscopy, followed by LCI. Biopsy samples were obtained from 24 cases and 36 specimens. We focused on acute inflammatory cell infiltration (ACI), chronic inflammatory cell infiltration (CCI), and crypt architectural irregularities (CAI) findings of inflamed tissues, and classified these as 0, 1, 2, or 3 based on severity. LCI was performed with non-magnified observation; those with a clear image of the submucosal vein were classified as LCI-C and those with an unclear image, where the whole image was observed as red, as LCI-U.

**Results:** Mayo endoscopic score 0, 1, and 2 according to the conventional endoscopic classification for LCI-C vs. LCI-U were 79.2%, 20.8%, and 0% vs. 0%, 66.7%, and 25.0%, respectively. Those classified as MR, MI, and MD according to magnifying chromoendoscopy classifications were 58.3%, 41.7%, and 0% vs. 0%, 50%, and 50%, respectively. Compared with biopsied tissue findings, the mean values of ACI, CCI, and CAI were 0.3, 1.2, and 0.8 vs. 0.9, 2.0, and 2.0, respectively. These results indicate that for both endoscopic and histological findings, the extent of inflammation in LCI-C was significantly lower than that in LCI-U.

**Conclusion:** LCI of UC in remission is sufficient to estimate the extent of inflammation in the mucosa, similar to conventional endoscopy and magnifying chromoendoscopy. The estimation of mucosal healing with LCI and magnifying chromoendoscopy is useful to predict the recurrence of UC in remission.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1382 PATENCY CAPSULE RETENTION IN IBD. IS IT ALWAYS DUE TO STRICTURES?

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**Introduction:** Capsule retention is one of the complications of Small bowel capsule endoscopy (SBCE). The patency capsule (PC) is a useful tool prior to SBCE as to identify those patients with a higher retention risk. The aim of our study was to determine the patency capsule retention in patients with IBD as compared to non-IBD patients.

**Aims & Methods:** Patients who had a patency capsule (2009–2014) were identified through a database. Their clinical notes were reviewed. Patients were followed for a minimum of 12 months post procedure.

**Results:** 148 patients, mean age being 37.8 years (8–78 years) (76.5% female) were recruited. 23% of patency capsules were retained. 11.8% of these had a repeat patency capsule which was retained as well. The main indication for patency capsule was IBD (38.2%). The rest were performed in the investigation of: anaemia (23.5%), familial polyposis (8.8%), abdominal pain (5.9%), coeliac disease,(5.9%) tufting enteropathy (5.9%), abnormal imaging of the small bowel (5.9%), eosinophilic gastroenteropathy (5.9%). There was no statistically significant difference between IBD and non-IBD patients for PC retention ($p = 0.128$, RR 1.08). As for the retained PC cohort, from the IBD subgroup, 61.5% of patients with normal CT or MR enterography retained the PC. In the non-IBD group, 76.2% with normal CT or MR enterography did not pass the PC. There was no statistically significant difference between the 2 groups ($p = 0.8$).

**Conclusion:** This study demonstrates a high PC retention rate in both groups compared to published data. In patients with IBD, small bowel disease which is not detected on CT or MR imaging may partially account for this. However, a slower transit time may also be responsible in both groups. A careful history together with use of prokinetics and bowel preparation may actually enable the PC to be excreted thus allowing for capsule administration. Furthermore, a PC should always be performed prior to SBCE in patients with IBD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1383 UTILITY OF C-REACTIVE PROTEIN (CRP) IN PREDICTING COMPLICATED DISEASE COURSE IN CROHN'S DISEASE

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**Introduction:** Crohn's disease (CD) is a progressive disorder with evolution of disease phenotype from inflammatory to a complicated disease course with stricturing or penetrating behaviour. Early identification of patients likely to develop a complicated disease course will result in better stratification for early, aggressive 'top-down' therapeutic strategy. Currently available clinical predictors (young age, smoking and extensive small bowel disease) have limited sensitivity. Biomarkers such as CRP have long been utilised to monitor both response to treatment and predict need for surgery in isolated ileal CD.(1)

**Aims & Methods:** In this study we sought to identify if CRP at presentation could predict early or late complications in CD. Patients with CD diagnosed at Royal Liverpool University Hospital between 2006 and 2014 were identified from a retrospective database. Those who had CT or MR imaging around time of diagnosis were included in this study. The CRP at diagnosis, smoking status, presence of complications on index and follow up imaging and time to complications were recorded for each case. Continuous variables were summarised as means ± standard deviation (SD) and categorical variables as frequencies. The predictive utility of CRP was examined using a multivariate logistic regression.

**Results:** A total of 81 patients were included in the study, mean age 41 (SD 17.2), of which 28 (35%) were men, 53 (65%) were women and 25 (31%) were smokers. Eighteen (22%) had complications (abscess, stricture) at diagnosis and 22 (35%) had complications at follow up (Median follow up 529 days). Neither smoking (odds ratio (OR) 0.53, 95% CI 0.13–2.18, $P = 0.4$) nor CRP (OR 1.0, 95% CI 0.99–1.01) predicted a complicated disease course at diagnosis. Similarly, smoking (OR 4.3, 95% CI 0.8–21.9, $P = 0.07$) and CRP (OR 1.0, 95% CI 0.99–1.01, $P = 0.36$) did not predict complicated disease course during follow up. However, presence of complications at diagnosis predicted complications at follow up (OR 28.6, 95% CI 4.5–181.2, $P < 0.001$).

**Conclusion:** In a retrospective cohort of CD patients CRP at diagnosis did not predict a complicated disease course in the short or long term. The study was underpowered to confirm that smoking predicts a complicated disease course, but the OR indicates it is likely to be so. Finally, presence of complications at diagnosis was predictive of a complicated disease course at follow up.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1384 RISK FACTORS FOR A DIAGNOSTIC DELAY IN IBD

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**Introduction:** The timely diagnosis of inflammatory bowel disease (IBD) is still an important challenge and takes several years in the western industrial countries. However, there is no explanation why it takes so long from first symptom to determine the correct diagnosis.
**Aims & Methods:** We evaluated risk factors and circumstances which would lead to a delayed diagnosis of Crohn's disease (CD) or Ulcerative Colitis (UC). 386 adult IBD patients (200 CD = 51.8%, 186 UC = 48.2%, 210 females and 176 males) visiting 3 IBD outpatient clinics of the University hospital Charité and the City Hospital Waldfriede were included in our study. We created a questionnaire to assess patient characteristics like gender, age, residence at diagnosis and we assessed disease dependant symptoms, disease intensity at onset and change of diagnosis. Furthermore we requested intervals from begin of symptoms to first medical contact and determination of diagnosis. Disease characteristics such as disease location, symptom intensity or leading symptoms were assessed. Data analysis was performed using the SPSS 22.0.
**Results:** The mean time from first symptom to diagnosis for all included IBD patients was 8 mo. UC patients were significantly faster diagnosed than CD patients (UC 4 mo. vs.12 mo., $p < 0.0001$). The time interval from first symptom to first physician contact by multivariate data analysis was significantly faster in patients suffering from UC compared to CD (1 mo vs. 2 mo, $p = 0.049$). The diagnosis of UC was mostly diagnosed by gastroenterologist (45.6%) whereas the diagnosis of CD was established during admission to hospital (45%). The faster diagnosis of IBD was made by general practitioners and during hospital admission (each 6 mo). Most frequently the diagnosis was established by colonoscopy (CD:78%, UC:96%). Males were significantly faster diagnosed than females (1.5 mo. vs. 3 mo.; $p = 0.027$). Age at diagnosis or year of diagnosis didn't lead to a diagnostic delay. Severity of symptoms at disease onset significantly influenced the time to diagnosis (UC: $p = 0.002$ and CD: $p = 0.033$). Surprisingly, the time to diagnosis in UC patients with affected family members was significantly longer compared to patients without affected family members (10 mo. vs. 4 mo., $p = 0.0012$). CD patients with affected family members contacted significantly faster a physician (0.5 mo vs. 2.5 mo., $p = 0.003$). Fever lead to a significantly shorter time to diagnosis, whereas the symptom exhaustion lead to a significantly longer time span to diagnosis ($p = 0.038$). Patients with flatulence waited significantly longer to contact a physician (HR 0.27; $p = 0.035$) whereas vomiting and nausea lead to a significantly faster physician contact (HR 1.39; $p = 0.019$). Patients with the leading symptom fistula waited significantly shorter to contact a physician (HR 3.19; $p = 0.013$). Whereas weight loss or skin involvement lead to a faster diagnosis (HR 15.4/6.5; $p = 0.01$ each), joint pain or abdominal pain lead to a delayed diagnosis (HR 0.3/0.7; $p = 0.027$/0.006). There was no correlation between time to diagnosis and residence of the patient. Only 20% of patients had ever heard from IBD. Interestingly, if patients knew about IBD they waited significantly longer to contact a physician compared to patient who never heard about IBD (3 mo vs. 1.4 mo, $p = 0.02$).
**Conclusion:** The delay of diagnosis of IBD is still an underestimated problem leading to a prolonged period of time were patients suffer from symptoms. Surprisingly, patients and physicians share the responsibility for the delay of diagnosis indicating the need for a better information system for physicians but also patients. Especially in context of the worsening of disease course with delay of diagnosis it is extremly necessary to optimize the diagnostic process and to shorten the diagnostic delay.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1385 RELATIONSHIP BETWEEN SERUM INFLIXIMAB TROUGH LEVELS AND LABORATORY PARAMETERS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

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**Introduction:** Anti-tumor necrosis factor (TNF)-α, infliximab, is a potent therapeutic option in patients with inflammatory bowel diseases (IBD) of moderate to severe activity. The trough level of anti-TNF-α shows a close relationship with maintained disease activity. Previous studies reported a correlation between serum infliximab trough levels and certain laboratory parameters (C-reactive protein [CRP], albumin) associated with disease activity and suggested a higher elimination rate of the drug by intense inflammation.
**Aims & Methods:** We aimed to investigate the correlation between serum infliximab levels and routine laboratory parameters in patients with inflammatory bowel disease. Blood samples were collected at random intervals from IBD patients before infliximab infusions (originator or biosimilar). Serum infliximab trough levels and antibodies against infliximab were determined with ELISA technique. Various laboratory parameters (including electrolytes, liver, kidney and pancreas function, albumin, CRP, iron, and qualitative blood count) were also measured.
**Results:** A total number of 170 blood samples were collected at random intervals from 64 IBD patients (mean age: 36 years; male/female ratio: 27/37; 25 patients with ulcerative colitis, 39 patients with Crohn's disease). Disease activity was recorded in 93 cases (55%). Dose escalation was necessary in 24 cases (14%). No infusion reaction was reported. Originator product was administered in 35 and biosimilar in 29 patients. The level of antibodies against infliximab was measurable in 30 cases (17.6%). The mean infliximab serum trough level was 6.595 ug/mL. As a result of multivariate analysis, serum infliximab trough levels were significantly lower in case of originator drug administration compared to biosimilar ($p = 0.0019$), in active disease ($p = 0.027$), and in the presence of antibodies against infliximab ($p < 0.0001$). Gender, age and dose escalation did not cause a significant difference in infliximab levels. No correlation was found between the serum levels of infliximab and any of the routine laboratory parameters.
**Conclusion:** As opposed to the literature we were unable to identify a correlation between serum infliximab trough levels and routine laboratory parameters such as CRP or albumin, and therefore no biochemical activity markers can substitute the determination of anti-TNF level.

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## P1386 ANAEMIA IN CROHN'S DISEASE – SHOULD WE ASSESS MUCOSAL HEALING IN PATIENTS IN CLINICAL REMISSION?

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**Introduction:** Anaemia is an important manifestation of Crohn's disease (CD) and arises, mostly, from iron deficiency or chronic inflammation. It is more common in patients with clinical activity, although it may manifest in sustained clinical remission (CR).
**Aims & Methods:** To determine the factors related to the development of anaemia in a group of patients with CD. One-year cross-sectional single-centre study (2015). Patients with CD followed in an Inflammatory Bowel Disease (IBD) outpatients clinic were evaluated; retrospective review by consulting a national IBD database and medical records. Definitions- anaemia: haemoglobin < 130 g/L in males and < 120 g/L in females; iron deficiency: ferritin < 30 mg/dL; CR: Harvey Bradshaw < 5; endoscopic remission (ER): SES-CD < =2 or Rutgeerts score < i2. Statistical analysis: SPSS V20 (Chi2, Fisher's exact test, Pearson correlation).
**Results:** 127 patients were evaluated, mean age was 47 years (19–85), 58.3% female; Montreal classification: A1/A2/A3: 8/89/30, L1/L2/L3: 44/15/61, L4: 8, B1/B2/B3: 55/31/41, perianal disease: 49; previous abdominal surgery: 52; 26% of the patients had anaemia (n = 33) and 32.3% iron deficiency (n = 41) - ongoing therapy: immunomodulators (IM): 16, anti-tumour necrosis factor (anti-TNF): 6, IM+anti-TNFa: 7, aminosalicylates alone: 4, corticosteroids: 5. Haemoglobin was inversely correlated with C-reactive protein, CRP, ($r = -0.210$, $p = 0.018$). 72.7% of patients with anaemia (n = 24) were in CR and only 5 in ER; MRI or CT enterography was done in 10 patients and 9 had radiographic changes. Factors associated with the development of anaemia were: presentation at diagnosis (anaemia or clinical findings similar to ulcerative colitis were more common, $p = 0.001$), elevated CRP ($p = 0.037$) and endoscopic activity ($p < 0.001$).
**Conclusion:** The development of anaemia in patients with CD, even in clinical remission, should prompt an early assessment of mucosal healing to optimize the therapeutic strategy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1387 RED FLAGS INDEX: VALIDATION AND CLINICAL UTILITY

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**Introduction:** The absence of specific signs and symptoms in Crohn's disease often cause delay in the diagnosis of inflammatory bowel disease. In this context, it was recently developed the "Red Flags"[1] index, whose purpose is early hospital referral of patients with suspected Crohn's disease.
**Aims & Methods:** Validation of Red Flags index. Retrospective study, considering all patients referred to the query of inflammatory disease, with suspected Crohn's disease between May 2012 to October 2015. "Red Flags" index was calculated, based on the information provided in the first consultation. After diagnostic investigation, crohn's disease was confirmed in some patients and excluded in others. Original cut-off ($\geq 8$) of the red flags index was used.
Statistical analysis (SPSS v20.0): chi-square, t-student, sensitivity, specificity, negative and positive predictive (NPV/PPV) value and area under the curve (AUROC).
**Results:** Considering 91 patients (female: 59.8%, mean age 37 years), Crohn's disease was confirmed in 53.3% ($n = 49$). In 47.3% ($n = 43$), Red Flags index was above 8. The Red Flags index value of $\geq 8$ was associated with the presence of crohn's disease ($p < 0.01$). The original cut off demonstrated a sensitivity, specificity, PPV, NPV for the diagnosis of Crohn's disease of 73.5%, 83.3%, 83.7%, 72.9% (AUROC: 0.80), respectively.
**Conclusion:** The Red Flags Index is associated with the presence of Crohn's disease. The cut off $\geq 8$ showed a good diagnostic capacity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1388 SOLUBILE TRANSFERRIN RECEPTOR IN DIAGNOSIS OF IRON DEFICIENCY ANEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Soluble transferrin receptor (sTfR) is a dimer protein, and it represents a cleaved extracellular portion of the transferrin receptor 1. Levels of sTfR are related to iron status, and can be used in diagnosis of iron deficiency anemia (IDA), and differentiation from anemia of chronic disease (CDA). Although there are well-known and used markers for differential diagnosis of anemia, such as ferritin, there usage in inflammatory conditions is questionable due to its behavior as acute-phase reactant.
**Aims & Methods:** The aim of our study was therefore to clarify the correlation of sTfR and biochemical, pathohistological and endoscopic findings of patients with inflammatory bowel disease (IBD). A cross-sectional study was preformed among 30 patients with IBD. All patients underwent a total colonoscopy with ileoscopy. Complete blood count was obtained prior to the procedure in addition to inflammatory markers (CRP, erythrocyte sedimentation rate-ESR). 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.
**Results:** Sixteen patients had ulcerative colitis (UC) and fourteen patients had Crohn's disease. Our results showed that there was no statistically significant difference in all examined parameters (Hemoglobin, MCV, ferritin, CRP, ESR, Iron, TIBC, UIBC, sTfR) between these two groups of patients ($p > 0.05$). There was statistically significant negative correlation between values of Iron, TIBC and sTfR ($p < 0.05$). There was no statistically significant correlation between values of sTfR and disease activity presented by Mayo score, CDAI, endoscopic and pathohistological findings ($p < 0.01$).
**Conclusion:** Our results suggest that sTfR can be a useful parameter for the detection of iron deficiency anemia in IBD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1389 UPPER ENDOSCOPY IN INFLAMMATORY BOWEL DISEASES (IBD): WHAT CONTRIBUTION?

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**Introduction:** IBD mainly affect the colon, the ileus, the jejunum, and the anopérineal area. The systematic search for lesions in the upper digestive tract is still controversial. Nevertheless, it seems that two-thirds of patients who suffer from Crohn's disease and the half of those who have ulcerative colitis may have macroscopic and microscopic abnormalities in their upper gastro intestinal tract. Furthermore, an association between IBD and celiac disease has been described.
**Aims & Methods:** We aim to determine the role of upper gastro intestinal endoscopy in IBD. This is a retrospective descriptive study, including 59 patients who were followed in gastro intestinal department of our University Hospital, and who have had an upper endoscopy. We specified epidemiological, endoscopic and histological features.
**Results:** Among 160 patients who have an IBD, 59 have been included. The mean age was 35 years (range: 17 -68 years). 31 patients (52.5%) had Crohn's disease, 24 patients (40.6%) had ulcerative colitis, and 5 patients (9%) had indeterminate colitis Upper endoscopy was systematically performed in 55 (%) patients, and was indicated for investigation of upper gastro intestinal disorders in 7% (4 patients). It was normal in only 6 patients (10%) and revealed: oesophageal involvement in 5% (3 patients), erythematous antritis in 26 patients (44.4%), congestive fundite in 8 patients (13.5%), ulcerative bulbite in 5 patients (8.4%), atrophic appearance of the duodenal mucosa in 4 patients (6.7%), and aphthoid gastro duodenal ulceration evoking an upper localization of Crohn's disease in 3 patients. Histology allowed the confirmation of Crohn's disease in 12% (4 patients) and highlighted villous atrophy in 5% (3 patients). *H. pylori* was detected in 53% (31 patients). In our study, upper endoscopy was pathological in 89%, it could make the diagnostic of an upper localization of Crohn's disease in 12% among all patients who have Crohn's disease, and an association between Crohn's and celiac disease in 3.3% among all IBD patients.
**Conclusion:** Our study prove that realizing a systematic gastroscopy for all IBD patients is far from being profitable. However, its realizing in symptomatic patients or in case of diagnostic problem (Crohn's Disease, ulcerative colitis?) is much more justified and useful.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1390 SCREENING FOR DYSPLASIA AND COLORECTAL CANCER IN ULCERATIVE COLITIS: AN ALGERIAN STUDY

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**Introduction:** Patients with longstanding extensive ulcerative colitis have an increased risk of colorectal cancer.
**Aims & Methods:** The aims of this study were to determine the incidence of dysplasia and colorectal cancer, in patients with longstanding ulcerative colitis. We also evaluated prospectively, the proportion of dysplastic lesions detected by chromoendoscopy from targeted biopsies of macroscopically visible abnormalities, as opposed to random biopsies of colonic mucosa. In this prospective study, consecutive patients with clinically inactive, longstanding UC (8 years) were recruited from 4 centers; colonoscopy with chromoendoscopy using 0.1% methylene blue was performed for each patient. Four mucosal biopsy specimens were taken every 10 cm between the coecum and the rectum, with additional biopsies or removal of any abnormality mucosal. All the endoscopies were performed by a single endoscopist, all the biopsies have been reviewed by a pathologist experienced in gastroenterology.
**Results:** 224 chromoendoscopy were performed in 106 patients. We diagnosed 49 neoplastic lesions in 31 patients; there were 6 adenocarcinomas, 8 high-grade dysplasia, 24 low-grade dysplasia, and 11 lesions indefinite for dysplasia We did 8035 random biopsies witch found 7 dysplastic lesions in 6 patients: 1 high-grade dysplasia, 2 low-grade dysplasia and 4 lesions indefinite for dysplasia.

Random biopsies alone diagnosed dysplasia in 2 patients (1.8%), and had clinical impact only in one patient (0.9%).
**Conclusion:** The risk of colorectal cancer in Algerian ulcerative colitis patients is high. Colonoscopic surveillance is actually the only way to detect colorectal cancer at an early stage in ulcerative colitis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1391 NATURAL HISTORY OF NON SEVERE ULCERATIVE COLITIS AT DIAGNOSIS

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**Introduction:** The clinical course of ulcerative colitis (UC) may range from a quiescent course with prolonged periods of remission to severe disease requiring intensive medical treatment or surgery. Few data are available for the prevalence and the factors associated with long-term non-severe UC.
**Aims & Methods:** We aimed to assess the natural history of non severe UC at diagnosis and to identify predictive factors of mild evolution over the long term. We conducted a retrospective observational study conducted in a university hospital including patients diagnosed with UC between January 2005 and December 2016. Non severe UC was defined as no requirement for immunosuppressants, anti-TNF and colectomy. Statistical analysis was performed using SPSS v21.0, and a p-value $< 0.05$ was considered statistically significant.
**Results:** Among 105 patients with UC, 78 (74%) had a non severe disease at diagnosis. There were 37 men and 41 women with a mean age of 36.2 years [range: 18–69 years]. The mean follow-up period was of 7.8 years. Nineteen patients (24.4%) had acute severe colitis after a mean period of 40.8 months. Four patients (5.1%) required colectomy. Immunosuppressants were needed in 19 cases (24.4%) and anti-TNF in 2 cases (4.6%). Forty-nine patients (62%) had a non severe disease at the maximum follow-up. Long term non severe UC was significantly associated with the distal location of disease ($p = 0.001$) and the absence of corticosteroid therapy during the first year ($p = 0.002$).
**Conclusion:** In our series, nearly 1/3 of UC with non severe disease at diagnosis became severe with time. Absence of steroid use during the first year and distal location of disease were predictors of a long term non severe outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1392 EVALUATION OF PATIENTS WITH QUIESCENT CROHN'S DISEASE BASED ON CAPSULE ENDOSCOPY CROHN'S DISEASE ACTIVITY INDEX (CECDAI)

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**Introduction:** Crohn's disease (CD) patients with no symptoms and negative inflammatory markers still may be at risk of relapse. Capsule endoscopy (CE) allows convenient visualization and scoring of the mucosal condition at sites of small bowel lesions in CD patients. However, in many patients with no symptoms and CE suggesting no activity together with negative inflammatory, indications for starting treatment are unclear. This study was to understand the long-term outcomes in such patients, to determine the indications for initiating treatment for CD based on CE.
**Aims & Methods:** Between July 2012 and December 2015, CE was undertaken in 80 patients with CD after patency was confirmed by a patency capsule. Twenty-five patients who required treatment within 3 months after CE were excluded, and eleven patients who had CDAI $\geq 150$ or CRP $\geq 0.5$ mg/dl were excluded, and 44 were evaluated. At CE, the Capsule Endoscopy Crohn's Desease activity index (CECDAI) was determined and the patients were divided into a CECDAI $\leq 3$ group ($n = 27$) and a CECDAI $\geq 4$ group ($n = 17$). The rationale for classification into two groups was as follows. A CECDAI score of 3.8 is believed to be equivalent to a Lewis score of 135; CECDAI $< 3.8$ and Lewis $< 135$ are considered normal (quiescent disease), while a CECDAI score of 5.8 is equivalent to a Lewis score of 790; CECDAI $\geq 5.8$ and Lewis $\geq 790$ indicate moderate to severe disease. Since the CECDAI score is calculated as an integer, a score of $\leq 3$ is normal in clinical setting.
**Results:** The included patients were 22 male, and 22 female, average age $39.8 \pm 15.9$ years. Likewise, the average duration of CD was $119 \pm 88$ months. In 13 patients, CD lesions were confined to the small intestinal, and 31 patients had small and large intestinal involvement. At CE, the CDAI score was $66 \pm 33$, albumin (Alb) $= 4.3 \pm 0.3$ g/dl, and C-reactive protein (CRP) $0.13 \pm 0.11$ mg/dl. There was no significant difference between the 2 groups with respect to age, disease duration, medications including corticosteroids biologics, immunomodulators, surgical history, haemoglobin, Alb, CRP, or CDAI score. However, the Kaplan-Meier survival analysis showed a significant difference between the CECDAI $\leq 3$ and the CECDAI $\geq 4$ groups ($P = 0.0358$, Wilcoxon test).
**Conclusion:** We found that significantly more patients with the CECDAI $\geq 4$ required treatment intensification, or needed to switch to an alternative treatment over the long-term after CE, even when CDAI or CRP was not high at the time of CE. Based on these observations, we believe that the justification for starting aggressive therapeutic intervention in the clinical practice setting is not clear, if the patient has no symptoms. In contrast, if a patient has a CECDAI score of $\geq 4$, diligent monitoring is warranted to suppress a likely CD flare up.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1393 CLINICAL EFFICACY OF THE TOLL LIKE RECEPTOR-9 AGONIST COBITOLIMOD IN ANTI-TNF-ANTIBODY TREATED AND NAIVE PATIENTS WITH MODERATE TO SEVERE ACTIVE ULCERATIVE COLITIS

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**Introduction:** In the COLLECT study the Toll like receptor (TLR-) 9 agonist cobitolimod (formerly known as DIMS0150, Kappaproct®) was evaluated for its therapeutic efficacy in ulcerative colitis patients refractory to conventional therapy.
**Aims & Methods:** In this post hoc analysis the clinical effects of cobitolimod were analysed in anti-TNF-antibody experienced versus naive patients with active ulcerative colitis. Cobitolimod was studied in a randomized, double blind, placebo-controlled, multicentre, pan-European trial named COLLECT in 131 patients with moderate to severe active ulcerative colitis defined by a CAI score of 9 and more. Patients were on mandatory steroid therapy and could be taking sulphasalazine, aminosalicylates, or thiopurines at stable doses. Patients were randomly assigned to receive two single doses of cobitolimod (30 mg) or placebo (in a 2:1 ratio) topically through the endoscope to the inflamed mucosa at baseline (week 0) and after 4 weeks (week 4). For this post-hoc analysis efficacy was studied using the secondary endpoint symptomatic remission (SR) (absence of blood in stool and mean weekly stools $< 35$) at week 4, 8 and 12. As endoscopic examination was performed at week 4 and 12 symptomatic remission in combination with mucosal healing (MH) defined as endoscopic Mayo score £1 were assessed at week 4 and 12. In the FAS (full analysis set) population 39% of the patients had received anti-TNF-antibody treatment before inclusion, which was discontinued at least 4 weeks before study enrolment, and 61% of the patients were anti-TNF-antibody naive.
**Results:** In the anti-TNF experienced patient population symptomatic remission was achieved in 16/26/29% of the cobitolimod vs. 6/12/18% in placebo treated patients at week 4/8/12, respectively. In the anti-TNF naive patient population symptomatic remission rates were higher with 42/56/52% in the cobitolimod vs. 19/39/42% in placebo treated patients at week 4/8/12, respectively. With respect to the endpoint symptomatic remission plus mucosal healing the anti-TNF experienced patient population showed remission rates of 10/23% for cobitolimod vs. 6/18% for placebo treated patients at week 4/12, respectively. In the anti-TNF naive patient population absolute remission rates for SR plus MH were again higher with 28/38% of the cobitolimod vs. 0/27% in placebo treated patients at week 4/12, respectively.
**Conclusion:** Those post-hoc results of the COLLECT study demonstrate that dual topical administration of the TLR-9 agonist cobitolimod is able to induce clinical remission both in anti-TNF-antibody experienced and naive UC patients. As expected, absolute remission rates in anti-TNF experienced patients are smaller, but with a similar effect-size to anti-TNF naive patients compared to placebo treated patients of the same subgroup. Therefore, the concept of TLR-9 activation is a promising and well-tolerated novel therapeutic option both for anti-TNF-antibody pre-treated and anti-TNF naive ulcerative colitis patients.
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## P1394 COST-UTILITY OF BIOSIMILAR INFLIXIMAB FOR THE TREATMENT OF FISTULISING CROHN'S DISEASE IN NINE EUROPEAN COUNTRIES

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**Introduction:** Biosimilar infliximab was authorized by the EU in 2013 for the treatment of active fistulising Crohn's Disease (CD).

**Aims & Methods:** Our aim was to analyze the cost-effectiveness of biosimilar infliximab (by Hospira UK) in Belgium, France, Germany, Hungary, Italy, The Netherlands, Sweden and in the United Kingdom. A Markov model was developed to assess the cost-utility of biosimilar infliximab, as well as of treatment sequences involving three biologicals followed by standard care on a 5-year time horizon from the third party payers' perspective. Input data on effectiveness and health state utilities were obtained from the literature and assumptions were made if disease-specific data were not available. Country-specific costs and discount rates were considered. Uncertainty was assessed by one-way and probabilistic sensitivity analysis.

**Results:** Applying standard care as comparator scenario in all analyses, the incremental cost-utility ratio (ICUR) of biosimilar infliximab varied significantly across countries (from €24.785/QALY in Hungary to €52.235/QALY in Sweden) but was lower in each country compared to the originator drug (the lowest ICUR was calculated for Hungary: €49.286/QALY; and the highest for Germany: €96.494/QALY) and also compared to adalimumab (the lowest in France: €61.799/QALY; the highest in Germany: €136.118/QALY). The ICER of biosimilar infliximab-adalimumab-vedolizumab sequence (€51.506-€84.403/QALY) was lower in all countries than the same sequence with the originator infliximab (€65.612-€107.199/QALY), and was also lower than of adalimumab-biosimilar infliximab-vedolizumab strategy (€53.337-€88.050/QALY). Results of biosimilar infliximab-adalimumab-vedolizumab treatment sequence were the most sensitive to the perspective of the analysis, utility weights and the time horizon. Taking into account productivity loss, ICERs decrease by 4–25% across countries. A 10% increase in utility weights decreases the ICERs by 9% and a 10% decrease increases by 11% in all countries. On a 10-year time horizon ICERs decreases by 6–8%.The change of the assumption for biosimilar infliximab price from 50% of originator infliximab price to 40% and 60% ICERs change by 4–6%.

**Conclusion:** Applying biosimilar infliximab instead of the originator product is a cost-effective alternative that makes biological treatments more affordable and might facilitate access. Given the significant impact of utility weights on the results and the scarcity of available data, preference based quality of life studies focusing specifically on fistulising CD patients are encouraged in order to improve the validity of the analyses.

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P.L. Lakatos: PL Lakatos has served as a consultant for Celltrion, EGIS and Pfizer/Hospira and received speaker's honoraria from Celltrion, EGIS and Pfizer/Hospira and unrestricted research funding from Pfier/Hospira
All other authors have declared no conflicts of interest.

## P1395 BODY COMPOSITION PROFILE: A PREDICTOR OF THERAPEUTIC OUTCOME IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE

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**Introduction:** Anti-tumour necrosis factor (TNF) s form a major part of therapy in Crohn's disease with a primary non-response rate of 10–30% and a secondary loss of response rate of 5% per patient-year. BMI has been linked to primary non-response in observational cohort studies and may be due to pharmacokinetic effects on drug levels.[1] Myopenia is prevalent in patients with Crohn's disease who are in clinical remission and can be measured using body composition analysis tools.

**Aims & Methods:** The composition of a patient's body mass may demonstrate a more refined method of analysis and can predict for outcomes of anti-TNF primary non-response and secondary loss of response. Between January 2007 to June 2012, 650 anti-TNF-naïve patients underwent anti-TNF therapy for Crohn's disease in a single centre. Demographics including age, sex and BMI were collected. Patient's Montreal classification at diagnosis was identified. Primary non-response was defined as cessation of anti-TNF within 6 months of first administration as deemed by their treating gastroenterologist using global physician assessment. Secondary loss of response was defined as a recurrence of patient's symptoms after a period of improvement with subsequent need for cessation or switch of anti-TNF therapy. CT images were analysed for body composition parameters and used to estimate body fat-free mass. The outcome measures were primary non-response and secondary loss of response. COX-regression analysis was used to predict for outcomes with three-year follow-up data. A hypothetical dose of 5 mg/kg was delivered with estimated tissue levels.

**Results:** Of the 650 patients with anti-TNF therapy, 106 were included. 26 (24.5%) were primary non-responders and 29 (27.4%) had secondary loss of response. 13 patients were obese (BMI $>30$). Sex-specific cut-offs that defined a significant association between low muscle, high visceral fat and myosteatosis with outcomes were ascertained by stratification analysis. There were 26 patients (24.5%) who experienced primary non-response. Of these, 15 (57.7%) were myopenic. There were 6 (25%) patients with nonvisceral obesity and 5(25%) with myosteatosis. On multivariate analysis, myopenia predicted for primary non-response (HR4.74;1.81–12.39, $p=0.002$) to anti-TNF therapy (See Table 1). No other factors (visceral obesity, myosteatosis, age, gender and type of anti-TNF) were associated with LOR or PNR (Table 1). In patients with PNR, 15 (57%) were myopenic. In out cohort, 29 (27.4%) patients had secondary loss of response. The reason for the switch or cessation of anti-TNF therapy was due to recurrence in symptoms. Of the patients that had secondary loss of response, 7 (24.1%) were myopenic, 8 (27.6%) had visceral obesity and 5 (17.3%) had myosteatosis. However, on univariate analysis, there were no significant factors for prediction of secondary loss of response (Table 3). The association between estimated total body fat-free mass and BMI was poor ($r^2=0.15$). A consequence of high fat mass or low fat free mass would be a larger volume of distribution of anti-TNF therapy. A hypothetical dose of anti-TNF at 5 mg/kg of body weight was administered with calculated variations in the resulting anti-TNF per kg estimated fat-free mass. The overall distribution of estimated anti-TNF per kg fat-free mass varied greater than six-times (range 14.36– 97.92 mg anti- TNF per kg). Men were more likely to have a lower fat-free mass in proportion to their BMI than women ($p=0.05$), and thus a larger proportion of men than women were in the highest ranges of anti-TNF per kg fat-free mass.

**Table 1:** The relationship between PNR and clinico-pathological parameters

| | | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|---|
| | | OR 95% CI | p-value | OR 95% CI | p-value |
| **Gender** | Male | 1 | | | |
| | Female | 1.37 (0.56–3.40) | 0.488 | | |
| **Age** | (b = -0.002) | 0.99 (0.96–1.03) | 0.910 | | |
| **Myopenia** | Absent | 1 | | 1 | |
| | Present | 4.69 (1.83–12.01) | **0.001** | 4.73 (1.81–12.39) | **0.002** |
| **BMI** | BMI < 30 | 1 | | | |
| | BMI > 30 | 0.52 (0.11–2.52) | 0.420 | | |
| **Visceral Obesity** | Absent | 1 | | | |
| | Present | 1.03 (0.36–2.96) | 0.951 | | |
| **Mysoteatosis** | Absent | 1 | | | |
| | Present | 1.13 (0.33–3.17) | 0.923 | | |
| **Myopenic Obesity** | Absent | 1 | | | |
| | Present | 0.52 (0.11–2.53) | 0.420 | | |
| **Anti TNF drug** | Infliximab | 1 | | 1 | |
| | Adalimumab | 0.32 (0.10–0.98) | **0.048** | 0.31 (0.09–1.06) | 0.061 |

**Conclusion:** For patients with CD, certain BC profiles may demonstrate predictive effect on treatment responses. Our study has identified myopenia as a significant predictor of primary non-response of anti-TNF therapy in Crohn's patients. Adjusting dosage and undertaking a holistic management approach with nutrition and muscle-building exercises may improve therapeutic outcomes in patients commencing anti-TNF therapy.

**Disclosure of Interest:** N.S. Ding: Advisory board - FALK and Abbvie
All other authors have declared no conflicts of interest.

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## P1396 PLACENTAL MADCAM1 EXPRESSION – POTENTIAL CONSEQUENCES FOR THE TREATMENT WITH VEDOLIZUMAB DURING PREGNANCY

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**Introduction:** Inflammatory bowel diseases (IBD) affect patients in reproductive age. Over the past two decades, the experience with the treatment of IBD during pregnancy has been increasing and most of the IBD drugs have been shown to be effective and safe for the use by the mothers-to-be. Vedolizumab, a monoclonal antibody against alpha4beta7 integrin has been shown to be effective in inducing and maintaining remission in IBD. By blocking alpha4beta7, it is preventing the homing of lymphocytes to the gut mucosa through binding to mucosal vascular adressin cell adhesion molecule 1 (MadCAM1) localised on the endothelial cells. As with other biologicals in the past, the question arises on the safety of the use of this novel molecule during pregnancy. Embryonic implantation is a complex process orchestrated by maternal immune response. It is not clear whether MadCAM1 is expressed in human placenta which could have consequences for the local immune response during pregnancy in case of alpha4beta7 blockade. Therefore, the aim of this study was to determine the expression of MadCAM1 in the placental tissue.
**Aims & Methods:** Placental tissue of 15 placenta's from spontaneous abortions occurring during the first trimester and 12 mature placenta's were stained by immunohistochemistry for the expression of MadCAM1. The localization of positive cells was determined based on the comparison with the hematoxylin-eosin staining. Samples from small intestinal wall were used as positive controls.
**Results:** MadCAM1 was expressed invariably by decidual vessels, syntiotrophoblast and cytotrophoblast in all samples from the first trimester. In contrast, there was no expression of MadCAM1 in the samples from mature placenta's.
**Conclusion:** MadCAM1 is expressed in human placenta during the first trimester. Blocking alpha4beta7 integrings may thus interfere with the maternal immune surveillance crucial for the successful course of early stages of the pregnancy.
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## P1397 NOVEL BUDESONIDE SUPPOSITORIES VERSUS GOLD STANDARD MESALAZINE SUPPOSITORIES FOR ACTIVE PROCTITIS. A PROSPECTIVE, DOUBLE BLIND, RANDOMISED TRIAL

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**Introduction:** Topically acting mesalazine suppositories are the gold standard for the treatment of active proctitis. In some patients, alternative treatment options are needed.
**Aims & Methods:** To compare the efficacy and safety of two different dosages of a novel budesonide suppository vs a mesalazine suppository vs a combination treatment of budesonide/mesalazine suppositories in active ulcerative proctitis (modified UC-DAI 4–10, with endoscopic subscore $\geq$ 1). This was a prospective, double-blind, double-dummy, randomised, multicenter Phase II trial in 337 patients (ITT population) with active proctitis, comparing the following 4 different suppository treatment arms over 8 weeks: budesonide 2 mg (BU2; n = 89 patients), budesonide 4 mg (BU4; n = 79), mesalazine 1000 mg (ME; n = 81); BU2 plus ME (BUME; n = 88). Primary endpoint was the time to resolution of clinical symptoms defined as the first day of 3 consecutive days with a score of 0 for rectal bleeding and stool frequency.
**Results:** Mean time to resolution of symptoms was [days] 35.5 in BU2, 29.8 in BU4, 29.2 in ME and 29.3 in BUME (BU2 vs BUME, p = 0.032; BU2 vs ME, p = 0.046). Clinical remission (modified UC-DAI subscores "rectal bleeding" and "stool frequency" = 0) occurred in 49.4% of patients in BU2, 57.0% in BU4, 66.7% in ME and 58.0 in BUME; BU2 vs ME ($p < 0.05$). Endoscopic remission (modified UC-DAI subscore < 2 AND at least 1 point reduction) was observed in 68.5% with BU2, 75.9% with BU4, 77.8% with ME, and 81.8% with BUME. 45.5% of patients improved histologically in BU2, 51.9% in BU4, 60.5% in ME, and 56.8% in BUME. Physician's and patient's global assessment was at least good in 68.5% and 71.9% with BU2, 81.0% and 84.8% with BU4, 82.7% and 87.6% with ME, and 90.9% and 89.7% with BUME, respectively. Majority of patients assessed administration of both suppositories as easy and did not have any preference. No serious adverse event and no unexpected adverse drug reaction occurred in the study.
**Conclusion:** BU4 was more efficacious than BU2 and similarly efficacious than the standard ME. The combination treatment BUME did not result in major advantages compared to BU or ME monotherapy in this patient population. BU4 appears to be an effective and safe novel treatment option for proctitis.
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A. Dorofeyev: Received lecture fees and travel costs by Dr. Falk Pharma, Germany.
R. Mohrbacher: Received salary (employment) by Dr. Falk Pharma, Germany.
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B. Siegmund: Received lecture fees and travel costs by Dr. Falk Pharma, Germany.
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## P1398 VSL#3 IS NO LONGER VSL#3 IN CONTINENTAL EUROPE: WARNING FOR DOCTORS AND PATIENTS

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**Introduction:** The probiotic mix VSL#3 has built strong scientific evidence over the last 2 decades and is recognized by main Gastroenterology Associations (AGA, ECCO) for the prevention of onset and maintenance of pouchitis as well as for Ulcerative Colitis. Recently, a formulation produced by a different manufacturer (therefore different from the original formulation) has been launched under the same brand VSL#3 in Italy, Holland and sporadically in the UK., causing confusion to healthcare providers and patients regarding safety and efficacy.
**Aims & Methods:** Viability and functional expression of probiotic bacteria are influenced by a variety of external factors, including fermentation conditions (i.e. micronutrients, pH etc.), method of concentration and method of stabilizing the culture, including storage conditions. These changes impact on the numeric recovery of live /dead bacterial cells and their effect on host biomarkers, such as immune cells, anti-inflammatory profile, and biochemical patterns. (1,2,3). The "original VSL#3" formulation endorsed by the Guidelines was therefore compared with the "new VSL#3" formulation. The live/dead status of bacteria was assessed using a mixture of SYTO® 13 green fluorescent nucleic acid stain (live bacteria) and the red fluorescent nucleic acid stain, Propidium Iodide (PI) (dead bacteria). The two formulations were also tested on different cell lines for DNA cycle and cell apoptosis.
**Results:** The "new VSL#3" has 233% more dead bacteria than the "original VSL#3". The percentage of dead bacteria in the single sachet is an important parameter since: (a) it is a good predictor of the quality of the product and its shelf life stability, and (b) "dead bacteria" are biological response modifiers. The two formulations are also different when tested on different cell lines. The "original VSL#3" influences cell cycle profile differently when compared to the "new VSL#3", in particular in its capability to arrest the cells in G0/G1 phase and in inducing the apoptotic death. Consistent with the increased apoptosis, a statistically significant reduced number of cells treated with the "original VSL#3" is observed in the G2 phase when compared to the "new VSL#3" and correlates with a reduced proliferative index of cells treated with "original VSL#3" compared to "new VSL#3". Since this test is the final outcome of a very complex cascade of a number of immunological and biochemical pathways activated by the bacteria present in the formulation, the results are relevant for IBD patients who, because of their chronic inflammatory state, are at high risk of cancer.
**Conclusion:** These preliminary assessments confirm that the "new VSL#3" is different from the "original VSL#3" thus impacting the specific activity, synergy and characteristics of this complex bacterial blend. Doctors and patients must be informed that all previous studies, clinical experiences and recognition by AGA and ECCO cannot translate to the "new VSL#3" and thus imposes the need for proper assessment of the safety and clinical efficacy of the "new VSL#3".
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1399 CALPROTECTIN IS LESS ACCURATE THAN MAYO ENDOSCOPY SCORE TO MONITOR CONTINUOUS CLINICAL RESPONSE IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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**Introduction:** Continuous clinical response (CCR) is an endpoint applied in the PURSUIT maintenance (M) trial to reflect the performance of patients over time.[1] Calprotectin is a faecal marker highly associated with mucosal inflammation in ulcerative colitis (UC).[2]

**Aims & Methods:** We investigated whether change of calprotectin levels during follow-up of UC patients taking golimumab Q4W can replace endoscopy as an objective measure of disease activity in UC. This is a post-hoc analysis of the PURSUIT-M trial, whose primary endpoint was CCR, defined as sustained clinical response assessed by partial Mayo score Q4W and Mayo score at weeks 30 and 54.[3] We compared the association of CCR with the Mayo endoscopy score (at weeks 30 and 54) to the association of CCR with the change of calprotectin levels from pre-induction baseline to weeks 30 and 54. CCR implies Mayo response, including endoscopic response at weeks 30 and 54; therefore weeks 30 and 54 endoscopic score were used as the reference to test the accuracy of calprotectin change. Comparative evaluation of receiver-operating characteristic curve AUC data was performed using the DeLong method.[4]

**Results:** The Mayo endoscopy score at weeks 30 and 54 was highly associated with CCR through 54 weeks: AUC of 0.83 and 0.90, respectively (**Table**). Compared to the Mayo endoscopy score as the reference, the association (AUC) of change of calprotectin levels from baseline to weeks 30 and 54 was 0.66 and 0.64, respectively. At both weeks 30 and 54, change of calprotectin levels from baseline was significantly less accurate than the Mayo endoscopy score in predicting CCR ($P < 0.0001$ for both weeks 30 and 54).

| Testing for Association with CCR | Change of Calprotectin Levels From Baseline | Mayo Endoscopy Score |
|---|---|---|
| Week 30 (n = 432) | | |
| AUC | 0.6605 | 0.8308 |
| Difference | −0.1703 ($P < 0.0001$) | reference |
| Sensitivity/Specificity | 0.73/0.57 | 0.89/0.73 |
| Week 54 (n = 428) | | |
| AUC | 0.6389 | 0.8979 |
| Difference | −0.2589 ($P < 0.0001$) | reference |
| Sensitivity/Specificity | 0.65/0.58 | 0.91/0.84 |

AUC=area under the curve.

**Conclusion:** Change of calprotectin levels from baseline to weeks 30 and 54 in PURSUIT-M less accurately predicts CCR compared to the Mayo endoscopy score. Although early change in calprotectin levels (from baseline to week 6 of PURSUIT induction) is a predictor of CCR,[5] its accuracy to monitor CCR during maintenance is lower than that of endoscopy. Our data thus support endoscopy as the superior objective assessment of mucosal activity in UC versus calprotectin, which can be considered an adjunctive biomarker as suggested in the STRIDE consensus.[1]

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## P1400 THE COMBINED CELL AND ANTICYTOKINE THERAPY PROMOTES DEEP REMISSION OF CROHN'S DISEASE

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**Introduction:** Anticytokine therapy with anti-TNF-a drugs contributes to deep remission of Crohn's disease (CD). At present, for the treatment of CD used mesenchymalstem cells (MSCs). Simultaneously, MSCs, patients receiving concomitant immunosuppressivetherapy. At the present time has not been studied clinical efficacy of combined use of MSCs and anti-TNF-a drugs in the treatment of patients with CD.

**Aims & Methods:** We aimed to examine the efficacy of combination therapy of mesenchymal stem cells (MSCs) of bone marrow, and infliximab (IFX) to achieve immunobiological and histological remission in patients with Crohn's disease. Methods: Sixty-seven patients with CD (colitis and ileocolitis) divided into 3groups. The first group of patients CD (n = 21) received standard anti-inflammatory therapy + MSCs. The second group (n = 30) received therapy anticytokine IFX. A third group of patients with CD (n = 16) received anticytokine therapy IFX + MSCs. Immunobiological effectiveness of the therapy was evaluated by the level of CRP and fecal calprotectin (FCP) and pathomorphological assessmentwas evaluated by index of Geboes. Evaluation of efficacy was performed after 2,12 and 24 months after initiation of therapy. Baseline CRP in acute disease ingroup 1 was 24.0 6 1.9 mg/L in the 2nd—22.5 6 2.1 mg/L ($P = 0.37$) in 3rd—23.06 2.4 mg/L ($P = 0.47$). Baseline FCP in the 1st group was 804.8 6 88.8 mg/g, inthe 2nd—848.3 6 83.9 mg/g ($P = 0.09$), in the 3rd—937.5 6 125.6 mg/g ($P = 0.006$). The index of Geboes in the 1st group was 4.4 6 0.2 points, the 2nd—4.356 0.2 points ($P = 0.11$), in the 3rd—4.6 6 0.3 points ($P = 0.002$).

**Results:** After 2 months, the level of CRP in patients in the 1st group was 9.8 6 1.1 mg/Lin the 2nd—8.4 6 1.3 mg/L ($P = 0.14$) in 3rd—7.9 6 0.9 mg/L ($P = 0.18$). The level ofthe FCP in patients in 1st group was 88.8 6 5.3 mg/g, in the 2nd—90.6 6 6.8 mg/g ($P = 0.001$), in the 3rd—68.8 6 3.3 mg/g ($P < 0.001$). The index of Geboes in the 1st group was 0.7 6 0.1 points ($P < 0.17$), in the 2nd—0.66 6 0.1 points, 3rd—0.5 6 0.06 points ($P < 0.001$). After 12 months, the level of CRP in patients in the 1st group was 7.95 6 0.2 mg/L in the 2nd—8.0 6 0.2 mg/L ($P = 0.39$) in 3rd—8.1 6 0.2 mg/L ($P < 0.11$). The level of the FCP in patients in 1st group was 85 6 5.0 mg/g, in the 2nd—95 6 3.5 mg/g ($P < 0.001$), in the 3rd group—75 6 5.0 mg/g ($P < 0.001$). The index of Geboes in the 1st group was 0.9 6 0.1 points in the 2nd—1.1 6 0.1 points ($P < 0.001$), in the 3rd group—0.8 6 0.1 points ($P < 0.001$). After 24 months the average level of CRP in patients in the1st group was 9.6 6 2.2 mg/L in the 2nd—9.4 6 1.1 mg/L ($P$ ¼ 0.67) 3rd—7.9 6 0.9 mg/L ($P = 0.004$). The level of the FCP in patients in 1st group amounted to 118.0 6 5.2 mg/g, in the 2nd—116.0 6 4.8 mg/g ($P = 0.17$) in the 3rd group—80.0 6 5.0 mg/g ($P < 0.001$). The index of Geboes in the 1st group was 1.1 6 0.2 points, in the 2nd—1.1 6 0.1 points ($P = 1.0$), in the 3rd group—0.8 6 0.1 points ($P < 0.001$).

**Conclusion:** The combined mesenchymal stem cells and anticytokine anti-inflammatory therapy of CD contributes significantly deeper immunobiological and histological remission CD.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1401 EFFICACY, SAFETY AND LONG-TERM OUTCOME OF ENDOSCOPIC DILATION THERAPY FOR STRICTURING CROHN'S DISEASE OF THE UPPER GASTROINTESTINAL TRACT - A COMBINED ANALYSIS OF 127 ENDOSCOPIC BALLOON DILATION PROCEDURES

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**Introduction:** Strictures are a frequent complication of Crohn's disease (CD) and may occur in different segments along the gastrointestinal (GI) tract. In contrast to ileocecal strictures, endoscopic balloon dilation (EBD) for CD-associated strictures of the upper gastrointestinal (UGI) tract is rarely reported. We therefore performed a combined efficacy and safety analysis based on all published studies of EBD for UGI strictures available in the literature.

**Aims & Methods:** A formal systematic literature review was performed to assess all relevant citations found in Embase, Medline and the Cochrane library regarding EBD in upper GI CD. In addition our own unpublished data was included in this analysis. Upper GI tract was defined as esophagus, stomach and duodenum up to the ligament of Treitz. 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:** 13 publications with a total of 73 CD patients and 127 performed dilation procedures were included. Stricture locations were: duodenum n = 44, stomach n = 16 and esophagus n = 6. Technical success rate was 94.1%, resulting in clinical efficacy in 90.9% of patients. The mean maximum balloon caliber used for dilation was 18.9 mm. Major complications with regard to dilation, defined as perforation, bleeding or dilation-related surgery, occurred in 2.8% of all procedures. During a mean follow-up period of 25.5 months, 49.6% of patients reported symptomatic recurrence, while 54.2% of patients needed to undergo re-dilation and 31.3% required surgical intervention. The mean time to re-dilation was 7.4 months. 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 EBD for upper GI strictures in CD patients.
**Conclusion:** EBD for CD-associated strictures of the upper gastrointestinal tract has a high rate of short-term technical and clinical success with robust long-term efficacy and acceptable complication rates. Therefore, EBD should be considered as an alternative to surgery in patients with CD associated UGI strictures. Larger, controlled studies are needed to further evaluate EBD for upper GI strictures in CD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1402 SCREENING FAILURE RATES IN A LARGE CLINICAL TRIAL CENTRE FOR INFLAMMATORY BOWEL DISEASES: INCIDENCE, CAUSES AND CONSEQUENCES

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**Introduction:** Inflammatory bowel diseases (IBD) are chronic gastrointestinal disorders sometimes requiring introduction of investigational medical therapy in a clinical trial setting. Before enrolling in such a trial, patients must meet strict screening criteria. There is almost no data available on the incidence and causes of screen failure (SF), nor on the consequences of SF for these IBD patients.
**Aims & Methods:** We investigated incidence rates of SF over time in a tertiary IBD centre, identified the different (avoidable) causes, and explored the outcome of these patients. A review of all IBD patients screened for a sponsored double-blind placebo-controlled phase 1, 2 or 3 induction study between Jan 2009 and Dec 2015 was conducted at our tertiary IBD centre. Causes of SF were categorized into 6 groups: disease activity, haematology, chemistry, microbiology, protocol violation and withdrawal of consent. Thereafter, avoidable causes within each category were identified and defined as causes that could have been detected by detailed pre-screening (patient's medical history, previous lab reports, and current clinical disease activity). Finally, patient outcome was categorized into 5 groups: rescreening for the same clinical trial, screening for another trial, (re) introduction of conventional therapy, referral for surgery, or watchful waiting.
**Results:** During the 7-year study period, a total of 535 IBD patients were screened and 77 (14%) SF were identified in 37 different studies (78% female, median age 42 years, 56% Crohn's disease, 44% ulcerative colitis). SF rate clearly increased with time: 15% (9/61) in 2009, 7% (6/81) in 2010, 12% (10/83) in 2011, 8% (5/63) in 2012, 14% (14/98) in 2013, 23% (20/87) in 2014 and 21% (13/62) in 2015 (linear-by-linear p = 0.011). The most prevalent cause of SF was insufficient disease activity scoring (36% overall, 4% clinical and 32% endoscopic activity). Other causes were microbiology (22%), protocol violation (14%), withdrawal of consent (13%), deviation on chemistry (10%) or haematology (4%). Further analysis demonstrated that 23% (18/78) of SF could have been avoided: 4 patients with an inadequate clinical disease activity, 3 not meeting all exclusion criteria regarding previous medical history, 8 with deviations on chemistry and 3 on haematology. After SF, 21% (16/77) of patients could be rescreened and 14 of them were randomized in the same clinical trial, 21% (16/77) patients were screened for another trial, 42% (32/77) patients initiated conventional therapy, 6% (5/77) patients were referred for surgery, and 10% (8/77) patients did not receive further therapy.
**Conclusion:** Although the overall SF rate of 14% is considered acceptable, we observed a clear increase in SF rates in the last years. This increase is probably explained by more rigorous evaluation of endoscopic findings (central reading with strict endoscopic activity scoring). Indeed, while avoidable causes remained stable during the last 7 years, unavoidable causes (including endoscopic findings) increased. Nevertheless, approximately one-fifth of SF in IBD could have been avoided by thoroughly checking medical history, previous lab reports and current clinical activity scoring.
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All other authors have declared no conflicts of interest.

## P1403 TROUGH LEVELS AND ANTIBODIES TO USTEKINUMAB ARE NOT CORRELATED TO RESPONSE TO USTEKINUMAB TREATMENT IN CROHN'S DISEASE PATIENTS

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**Introduction:** Ustekinumab (UST), a monoclonal antibody against the p40 subunit of interleukin 12/13, is effective in Crohn's disease (CD) patients refractory to anti-TNF agents. Trough levels and anti-drug antibodies to anti-TNF have been shown to be correlated to response to anti-TNF treatment. The aim of the present study was to assess the association between UST trough levels and anti-ustekinumab antibodies, and response and remission to induction and maintenance UST treatment in CD patients.
**Aims & Methods:** We performed a prospective study including all CD patients refractory to anti-TNF who received subcutaneous (SC) UST from September 2015 to February 2016 in tertiary referral French center of Claude Huriez hospital in Lille. During induction, patients received 90 mg of SC UST at week 0, 4 and 12. During the maintenance phase, patients received 90 mg of SC UST every 8 weeks, which could be optimized by shortening injection interval to every 4 weeks in case of loss of response. Clinical response was defined by a decreased Harvey Bradshaw Index (HBI) by 3 points, clinical remission by HBI < 5, loss of response by new increase of HBI. UST trough levels and antibodies were dosed at 12 weeks, and at a single time-point for patients who had received more than 3 months of UST. The results of dosage were obtained by enzyme-Linked ImmunoSorbent Assay technique. We evaluated the correlation between clinical and biological response and remission to UST, and UST through levels and antibodies concentration. Differences between independent groups were traced with the use of the Mann–Whitney exact test.
**Results:** Twenty-seven patients with active disease received at least three SC UST injections and were prospectively included. At time of ustekinumab introduction, 60% of patients received concomitant immunosuppressant and 56% received corticosteroids. At the end of the induction phase (week 12), clinical response was observed in 64% patients. There was no significant difference in mean UST trough levels who responded to UST induction (median 1160 ng/ml; IQR: 568–1448) as compared to patients who did not respond (median 1740 ng/ml; IQR: 682–2968, p = 0.61). Sixteen patients (60%) received at least 4 injections of UST, with 5 patients who were optimized at the time of dosages. Clinical response was observed in 12/16 patients (75%). Median UST concentration in clinical responder was 1429 ng/ml (IQR: 649–19745), and 1522 ng/ml in non-responder (IQR: 1168–1759), with no significant difference in mean UST trough levels in two groups of patients (p = 0.95). UST trough levels were similar in patients in deep remission (3/27 patients, median UST concentration of 1252 ng/ml) and in patients who were not in deep remission (median 1429 ng/ml; p = 0.96). UST antibodies were undetectable in 0/27 patients.
**Conclusion:** We confirmed that UST treatment is effective in a majority of CD patients refractory to anti-TNF agents. Median trough levels to UST are not correlated to response and remission to UST induction and maintenance treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1404 HOSPITALISATIONS AND TREATMENT DISCONTINUATION AMONG PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE TREATED WITH VEDOLIZUMAB COMPARED WITH INFLIXIMAB

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**Introduction:** There is a dearth of real-world comparative-effectiveness studies of anti-integrins vs. anti-TNFs for the treatment of ulcerative colitis (UC) and Crohn's disease (CD). The objectives of this study were to compare IBD-related hospitalisations and time to discontinuation of 1st-line therapy among biologic-naïve patients with IBD treated with vedolizumab (VDZ) vs. Infliximab (IFX).
**Aims & Methods:** This retrospective study used data from 01/05/2014 to 16/02/2016 in the US Explorys Universe electronic health records database. Patients ≥ 18 years of age, diagnosed with UC (ICD-9 556.xx) or CD (ICD-9 555.xx), who initiated VDZ or IFX were included. Patients had ≥ 12 months of medical history prior to index, ≥ 180 days of follow-up, and were biologic-naïve. Patients initiating concomitant biologic therapies, and those who died were excluded. The date of the 1st infusion was defined as the index date. Patients initiating VDZ were propensity score matched (1:2) with those initiating IFX. Discontinuation was defined as no subsequent infusion of the index drug within 90 days of the previous infusion, treatment switch or add-on of another biologic agent. A Kaplan-Meier analysis was performed to assess the risk of discontinuation. The discontinuation rate difference was estimated using Cox regression analysis adjusted for 1:2 matching. The proportion of patients who experienced an IBD-related hospitalisation during the 180 days following the index date, as well as the overall mean rate of hospitalisations by treatment group (VDZ or IFX) were reported and tested for statistical differences.
**Results:** 91 biologic-naïve VDZ patients were matched to 182 biologic-naïve IFX patients. The average age in both groups was 44 years. 63.7% and 63.4% in VDZ and IFX groups were patients with CD, respectively, and 53.8% and

59.3% in VDZ and IFX groups were female, respectively. In the 6 months following treatment initiation, patients treated with VDZ showed a trend towards a lower risk of discontinuation compared with matched IFX patients (HR: 0.86 [95% confidence interval: 0.63, 1.16])). The proportion of patients with an IBD-related hospitalisation was numerically lower in the VDZ vs. IFX group (7.7% vs. 15.9%, P = 0.058) and the mean number of IBD-related hospitalisations was significantly lower for patients who were treated with VDZ vs. IFX (0.11 vs. 0.29, P = 0.048).
**Conclusion:** In real-world clinical practice among patients with UC and CD receiving 1st-line biologic therapy, those treated with VDZ showed a trend towards lower risk of treatment discontinuation and fewer IBD-related hospitalisations than patients treated with IFX. Further comparative effectiveness studies with larger samples and longer follow-up are required to confirm these findings.
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R. Wang: Employee of Evidera commissioned by Takeda Development Centre Europe Ltd. to conduct the study.
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## P1405 EXCESS STEROID USE IN IBD: TOO MUCH, HOW MUCH AND WHY? RESULTS FROM A NATIONWIDE AUDIT

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**Introduction:** Corticosteroids are the cornerstone of inducing remission in IBD but are limited in their ability to maintain remission, and associated with significant side effects. This is the first nationwide outpatient study of steroid use in IBD and factors affecting their use.
**Aims & Methods:** We audited consecutive IBD patients attending clinics at 11 centres over 3 months using a web-based assessment tool. Cases meeting criteria for steroid excess (SE) as defined by ECCO guidelines [1, 2] were blind peer reviewed and classified as non-IBD use, unavoidable and inappropriate steroid excess (ISE) according to standardised definitions. Associations between steroid use and patient and institutional factors were analysed.
**Results:** Of 1177 patients [48% CD, 49% UC, 3% IBD-U] 79% were in remission/mild disease, 18.5% had moderate and 2.5% severe disease. In the previous 12 months, 30% had received steroids, 13.8% had SE. Peer review revealed that SE was inappropriate in 51.2% of these (8% non-IBD use; 40.7% unavoidable). Excess steroid exposure was more common in patients with active UC compared to active CD (41.6% vs 26.6%; p = 0.02). In multivariate analysis, disease activity was a significant predictor of SE/ISE. In addition, being established on anti-TNF agents protected against SE and ISE in CD. Exposure to thiopurine (SE + ISE) and starting anti-TNF therapy (ISE) were associated with excess steroid use in UC. CD patients from centres with an IBD MDT were less likely to have SE, similarly CD patients in centres with combined surgical clinics were less likely to experience SE and ISE. Care in centres with dedicated IBD clinics was associated with less SE and ISE in patients with UC. Centres with large numbers of GI trainees showed higher rates of SE in UC and SE and ISE in CD. (All of above independent predictors on multi-variate with significance $p < 0.001$).
**Conclusion:** We identified inappropriate excess steroid use in 7% of UK IBD patients. Risk factors for steroid exposure differed between UC and CD, likely reflecting inter alia, differences in access to biologic drugs. Our study is the first to demonstrate positive effects of service configurations (IBD MDT, dedicated IBD clinics, combined surgical clinics) on treatment outcomes even after correction for differences in disease severity. There was an association between ISE in Crohn's and the number of GI trainees per centre suggesting possible gaps in training. Routine recording of excess steroid exposure is feasible and should be considered as a quality marker for outcomes of IBD services.
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## P1406 HOSPITALIZATION RISK AND REINTERVENTION AFTER ILEOCOLONIC RESECTION WITH ANASTOMOSIS IN PATIENTS WITH CROHN'S DISEASE. RESULTS FROM THE PRACTICROHN STUDY

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**Introduction:** 25% to 61% of patients with Crohn's disease (CD) will require intestinal resection during the first 5 years after diagnosis. Throughout the follow-up, operated patients can develop complications and require hospitalization or new surgeries. The aim of this study was to determine the incidence of hospitalizations and reinterventions in patients with CD undergoing ileocolonic resection with anastomosis.
**Aims & Methods:** PRACTICROHN was a retrospective study, including patients with CD aged ≥18 years-old from 26 centres who underwent ileocolonic or ileorectal resection with ileocolonic (or ileorectal) anastomosis between January 2007 and December 2010. Clinical, endoscopic and treatment data before and up to 5 years after surgery were retrospectively collected from medical records.
**Results:** 314 patients were analysed (mean age 40 years [SD 13], 48% men). Of these, 149 (51%) were smokers at the diagnosis and 115 (77%) at the time of surgery. Only 30 patients (9.5%) quitted smoking at the fifth year. Median time from CD diagnosis to surgery was 6 years (IQR 1–12). Indication for surgery was: 147 (48%) stenosing, 98 (32%) penetrating disease, 46 (15%) stenosing + penetrating and 14 (4%) refractoriness to medical treatment. 208 (68%) of patients received preventive therapy after surgery: 13% aminosalycilates, 9% antibiotics, 46% immunomodulators (IMM) and 1% anti-TNFs. During the follow-up, 56 patients (18%) needed at least one hospitalization during the first year, with median time of stay of 10 days (IQR 6–15). The reasons for hospitalization were: 36 (45%) recurrence or CD activity, 35 (44%) postoperative complications, 1 (1%) CD-related infection and 7 (9%) for other reasons. There was no CD cancer-related hospitalization. After 5 years 94 (30%) patients required hospitalization, most of them due to active disease. 45 (14%) required reintervention after 5 years, most of them (n = 23, 7%) during the first year, and the most frequent reason was postoperative complication (n = 18, 78%). Median time to first reintervention was 288 days (IQR 133–527).

| Hospitalizations, n (%) | 1–12 months n = 314 | 13–24 months n = 314 | 25–36 months n = 314 | 37–60 months n = 314 |
|---|---|---|---|---|
| **Total (accumulated)** | 56 (17.8) | 74 (23.5) | 82 (26.1) | 94 (29.9) |
| Previous surgery complication | 35 (11.1) | 48 (15.2) | 55 (17.5) | 63 (20) |
| Recurrence, CD activity | 36 (11.4) | 56 (17.8) | 72 (22.9) | 100 (31.8) |
| Neoplasia related to CD | 0 (0.0) | 0 (0.0) | 2 (0.6) | 5 (1.5) |
| CD related infection | 1 (0.3) | 2 (0.6) | 4 (1.2) | 8 (2.5) |
| Other | 7 (2.2) | 12 (3.8) | 16 (5.0) | 27 (8.5) |
| Total Reinterventions (accumulated) n (%) | 23 (7.32) | 33 (10.51) | 37 (11.78) | 45 (14.33) |
| Consecuence or complication of previous surgery | 18 (5.7) | 25 (7.9) | 28 (8.9) | 33 (10.5) |
| Related to CD | 10 (3.1) | 15 (4.7) | 17(5.4) | 22 (7.0) |
| Penetrating complication | 9 (2.8) | 13 (4.2) | 15 (4.7) | 19 (6.05) |
| Abscess | 5 (1.5) | 5 (1.5) | 6 (40) | 6 (1.9) |
| Mass | 1 (0.3) | 2 (0.6) | 2 (0.6) | 4 (1.2) |
| Fistulae | 5 (1.5) | 8 (2.5) | 9 (2.8) | 11 (3.5) |
| Perforating | 2 (0.6) | 4 (1.2) | 4 (1.2) | 4 (1.2) |
| Stenosing | 1 (0.3) | 1 (0.3) | 1 (0.3) | 3 (0.9) |
| Resistance to treatment | 1 (0.3) | 3 (0.9) | 3 (0.9) | 6 (1.9) |

**Conclusion:** During the CD-related post-surgery evolution, 1 in 5 patients will require hospitalization for disease recurrence or postoperative complications, and

1 in 14 will require a new reintervention after 5 years. Probably surgery centralization in experienced centres could minimize postoperative complications, and a more exhaustive postoperative prophylaxis could reduce complications for disease activity.

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L. Cea-Calvo: Full time employee for MSD Spain
B. Juliá De Páramo: Full time employee for MSD Spain
All other authors have declared no conflicts of interest.

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### P1407 ASSESSMENT OF IMPACT III WELL-BEING DOMAIN SCORES IN ADALIMUMAB-TREATED PAEDIATRIC PATIENTS WITH CROHN'S DISEASE


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**Introduction:** We assessed the impact of adalimumab (ADA) treatment on the well-being domain from the recently restructured IMPACT III questionnaire in patients (pts) enrolled in the IMAgINE 1 trial. The effect of ADA on emotional and social functioning domains has been reported previously.[1]

**Aims & Methods:** In IMAgINE 1, 6–17 years old pts with moderate to severe CD (baseline [BL] PCDAI >30) who failed or were intolerant to conventional therapy received ADA for 52 weeks (wks).[2] Escalation to blinded weekly (EW) ADA was allowed after wk 12 for pts with disease flare/non-response followed by open-label (OL) EW ADA for continued flare/non-response. Pts ≥10 yr at BL received the IMPACT III questionnaire; each individual question has five Likert response options (0 – 4); scores are then linearly transformed to a range of 0 to 100 for ease of data interpretation, with higher scores representing better HRQoL. Changes from BL in the well-being domain score and in individual IMPACT III questions at wks 12, 26, and 52 were reported. Prior infliximab exposure was used for subgroup analyses. Last observation carried forward (LOCF) was used for missing data (post-BL), pts who discontinued, or who moved to OL EW ADA.

**Results:** A total of 172 pts were analyzed: 55% were males, median PCDAI was 40, median CRP 1.2 mg/dL, and mean IMPACT III well-being score 46 at BL. 75 pts had prior exposure to infliximab. Mean well-being domain scores at BL for infliximab-naive and experienced pts were 49 and 44, respectively. Statistically significant improvements in well-being domain and individual questions scores were observed from week 12 and maintained to week 52 (Table). Overall well-being domain score at wks 12, 26, and 52 was 69, 68, and 68, respectively. Numerically higher changes from BL in well-being domain scores were seen in infliximab-naive pts compared with infliximab-experienced pts at wks 12, 26, and 52 (26, 27, and 25 vs 18, 16, and 16, respectively).

**Conclusion:** ADA treatment was associated with significant improvements in HRQoL in children with CD. Increases in well-being domain scores and individual question scores were maintained up to week 52 regardless of prior infliximab exposure.

| | | Mean change from baseline | | |
|---|---|---|---|---|
| | Mean baseline score | Week 12 | Week 26 | Week 52 |
| **Well-being domain** | 46 | 22*** | 22*** | 21*** |
| How much has your stomach been hurting you in the past two weeks? | 41 | 26*** | 25*** | 25*** |
| How often has your IBD prevented you from eating what you want in the past 2 weeks? | 45 | 20*** | 22*** | 22*** |
| How often have you been worrying about having a flare-up (increase of symptoms) in the last 2 weeks? | 48 | 22*** | 21*** | 20*** |
| How much energy did you have during the past 2 weeks? | 43 | 23*** | 23*** | 22*** |
| How often did you have to miss out on certain things (hobbies, play, parties) because of your IBD in the past 2 weeks? | 49 | 24*** | 25*** | 23*** |
| How often have you been bothered by diarrhea in the past 2 weeks? | 41 | 24*** | 23*** | 21*** |
| Did you have fun during the past 2 weeks? | 59 | 17*** | 16*** | 15*** |
| How often did you feel sick to your stomach in the past 2 weeks? | 47 | 23*** | 23*** | 21*** |
| How did you feel during the past 2 weeks? | 43 | 26*** | 23*** | 21*** |
| How tired have you felt in the past 2 weeks? | 37 | 25*** | 24*** | 23*** |
| Does your IBD get in the way of playing sports the way you would like to? | 43 | 17*** | 20*** | 21*** |
| In the past 2 weeks how often were you able to go to school? | 62 | 21*** | 19*** | 19*** |

***$p < 0.0001$ for mean change from baseline to weeks 12, 26, or 52 was based on a one sample t-test.

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## P1408 FRENCH PROSPECTIVE, LONGITUDINAL OBSERVATIONAL STUDY OF THE THERAPEUTIC MANAGEMENT OF MILD TO MODERATE ULCERATIVE COLITIS (OPTIMUM): FOLLOW-UP AT 3 YEARS

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**Introduction:** The aims of this study, set up in 2011, are to describe the progression and methods of therapeutic management of mild to moderate ulcerative colitis (UC) and to assess the remission rate and duration, as well as to determine the prognostic factors for relapse at 3 years.

**Aims & Methods:** 812 patients experiencing a flare-up of mild to moderate UC were enrolled by 130 gastroenterologists, 64% of whom are in private practice. The patient data are recorded in an electronic CRF during consultations conducted as part of regular follow-up. The finale and descriptive analysis of the data available as of 28 October 2015 is presented below and represents 494 (60.8%) patients who had a visit at least at 3 years.

**Results:** At 1 year, 527 (84%) patients were in remission of the UC flare which motivated inclusion. During the 3 years of follow-up, 417 (51.35%) patients had at least 1 relapse and 55 (7%) had at least 1 hospitalisation related to UC. At enrolment, 583 (72%) patients were receiving treatment for UC; 432 subjects were treated with oral 5-ASA, which was combined with rectal 4- or 5-ASA in 131 patients. At the consultation at 3 years, 379 (80.8%) patients were receiving treatment for UC; 273 patients were treated with oral 5-ASA. The ongoing treatment at each annual visit is presented in the following table. One notes an improvement of adherence as well as stability of the UCCS score over the 3 years of follow-up.

**Conclusion:** In this large prospective cohort of patients with mild to moderate UC, inducing remission and maintenance are mainly based on treatment with 5-ASA. At 3 years of follow-up, 72% of patients are treated with 5-ASA among 81% receiving a treatment for UC. 84% of the patients are in remission according to UCCS score and one notes an improvement in the treatment adherence over the 3 years of follow-up.

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F. Bahbah: Ferring pharmaceuticals

**Table:** Treatment, Adherence to the UC Treatment and UCCS Score for UC Activity

| Assessment at the visit | Inclusion (N = 812) | 1 year (N = 628) | 2 years (N = 533) | 3 years (N = 469) |
|---|---|---|---|---|
| **Ongoing treatment** | **583 (71.8%)** | **526 (83.8%)** | **445 (83.5%)** | **379 (80.8%)** |
| Oral 5-ASA | 432 (74.1%) | 394 (74.9%) | 341 (76.6%) | 273 (72.0%) |
| Corticosteroids | 91 (15.6%) | 34 (6.5%) | 29 (6.5%) | 18 (4.8%) |
| Immunosuppressants | 95 (16.3%) | 89 (16.9%) | 84 (18.9%) | 65 (17.2%) |
| Anti-TNF | 25 (4.2%) | 25 (4.7%) | 29 (6.5%) | 36 (9.5%) |
| **Adherence to UC treatment** | | | | |
| Completed self-assessment questionnaire* | 501 (85.9%) | 431(97%) | 318 (85.4%) | 268 (70.7%) |
| Good adherence | 114 (22.75%) | 120 (27.84%) | 119 (37.42%) | 107 (39.93%) |
| Moderate adherence | 213 (42.51%) | 178 (41.30%) | 119 (37.42%) | 89 (33.21%) |
| Poor adherence | 174 (34.73%) | 133 (30.86%) | 79 (24.84%) | 72 (26.87%) |
| **UCCS Score of UC Activity** | | | | |
| Absent | | 7 (1.11%) | 1 (0.19%) | |
| 0–2 Remission | 231 (28.45%) | 491 (78.18%) | 435 (81.61%) | 392 (83.58%) |
| 3–5 Mild activity | 344 (42.36%) | 81 (12.9%) | 59 (11.07%) | 52 (11.09%) |
| 6–10 Moderate activity | 236 (29.06%) | 49 (7.8%) | 38 (7.13%) | 25 (5.33%) |
| 11–12 Severe activity | 1 (0.12%) | | | |

*% calculated among subjects with ongoing UC treatment at the visit.

## P1409 A PILOT STUDY TO EVALUATE THE BENEFITS OF A RECRUITMENT PLATFORM, CT-SCOUT$^{TM}$ IN INFLAMMATORY BOWEL DISEASES (IBD) CLINICAL TRIALS: LINKING POTENTIAL PATIENTS TO CLINICAL TRIALS

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**Introduction:** Patient enrollment in clinical trials is the weakest link in the long and expensive clinical development process that brings new molecules to treat IBD and other disabling chronic diseases. It has been estimated that insufficient patient enrollment in clinical trials can double the clinical development time and in certain cases cause the trial to be prematurely terminated (1). The major reasons for poor patient recruitment is lack of study protocol knowledge together with the fear of a time-consuming process. The CT-SCOUT$^{TM}$ platform is a web-based device designed by the executive board of the GETAID - a French academic research group - that makes the clinical trials pre-screening, and inclusion process more efficient.

**Aims & Methods:** We conducted a prospective, single centre, open-label, observational pilot study. The objective was to evaluate the benefits of implementing the CT-SCOUT$^{TM}$ platform for patient enrollment into clinical trials within our tertiary-care, academic IBD centre. All physicians involved in the IBD centre were asked to use the CT-SCOUT$^{TM}$ platform on a daily basis to evaluate whether or not patients were eligible for either academic or industry-sponsored trials. The primary endpoint was the patient randomization rate per month. Characteristics of our IBD centre were noted on a prospective basis. The intervention period (Apr 2014 – Dec 2015) was compared with the previous 21-month reference period (Jul 2012 – Mar 2014) using Wilcoxon's matched-pair signed-rank test. Logistic regression analysis was performed to determine predictors of patient enrollment.

**Results:** After implementing CT-SCOUT$^{TM}$, the inclusion (Informed-consent form signature) and randomization rate increased from $1.7 \pm 1.4$ to $4.7 \pm 3.1$ ($p = 0.001$), and from $1.2 \pm 1.2$ to $3.5 \pm 2.8$ ($p = 0.005$) patients per month, respectively. During the 42-month study period, patient population grew in terms of both consultations and hospitalizations. The number of study coordinators and ongoing trials remained stable. See table.

| Characteristics (n per month, mean ± SD) | Before CT-SCOUT$^{TM}$ (Jul 2012 to Mar 2014) | With CT-SCOUT$^{TM}$ (Apr 2014 to Dec 2015) | P |
|---|---|---|---|
| IBD Consultations | $219 \pm 48$ | $270 \pm 57$ | 0.002 |
| IBD day hospitalization | $139 \pm 25$ | $189 \pm 32$ | 0.001 |
| IBD hospitalization | $15 \pm 6$ | $18 \pm 6$ | 0.13 |
| Physicians | $5.9 \pm 0.4$ | $6.4 \pm 0.7$ | 0.001 |
| Study-Coordinator | $1.6 \pm 0.5$ | $1.4 \pm 0.4$ | 0.09 |
| Academic study | $3.8 \pm 0.4$ | $3.7 \pm 0.5$ | 0.54 |
| Industry-sponsored study | $4.0 \pm 0.0$ | $4.5 \pm 0.7$ | 0.002 |

Using CT-SCOUT$^{TM}$ platform was predictor of a higher patient randomization in clinical trials (OR = 6.4, $CI_{95}$% [1.1–35.7], $p = 0.03$), as well as the increased consultation (20.4, 1.6–250.0, $p = 0.02$) and hospital patient populations (7.9, 1.3–50.0, $p = 0.03$).

**Conclusion:** Regardless of increasing the cohort of IBD patients followed in the centre, introducing CT-SCOUT$^{TM}$ has multiplied the patients recruitment rate in clinical trials by a three-fold factor in both academic and industry-sponsored clinical trials. CT-SCOUT$^{TM}$ appears to be a promising and easy-to-use web-based solution to the global issue of patient enrollment in clinical trials, considerably reducing clinical trial duration, therefore allowing new drug candidates to be registered more quickly and be made available to patients earlier.

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C. Stefanescu: Stock ownership in CTMA; Honoraria from MSD
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## P1410 SWITCHING OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE FROM ORIGINAL INFLIXIMAB (REMICADE®) TO BIOSIMILAR INFLIXIMAB (REMSIMA™) IS EFFECTIVE AND SAFE – ONE-YEAR FOLLOW-UP

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**Introduction:** Biosimilar infliximab (IFX) seems to have similar efficacy and safety to original preparation in patients with inflammatory bowel diseases (IBD) who are naive to anti-TNF therapy. However, the evidence on switching from original to biosimilar preparation is very sparse.

**Aims & Methods:** Our aim was to evaluate efficacy and safety of switching from original to biosimilar IFX in patients with Crohn's disease (CD) and ulcerative colitis (UC) one year after the switch. Consecutive patients with CD and UC on maintenance IFX treatment in our centre who were switched from original to biosimilar IFX during period from January to March 2015 were included. Patients were followed prospectively in regular intervals coincident with infusion applications. At each visit disease activity was registered using Harvey-Bradshaw index (HBI) for CD and Simple clinical colitis activity index (SCCAI) for UC; blood sample was taken for analysis of blood count, biochemistry and IFX pharmacokinetics (trough levels, TL and anti-drug antibodies, ATI) and stool samples were collected for measurement of fecal calprotectin (FC). Furthermore, adverse events were registered. All patients were evaluated at week 56 (W56) of treatment with biosimilar IFX.

**Results:** Seventy-four patients with IBD, 56 with CD and 18 with UC, were switched to biosimilar IFX after mean time of $3.0 \pm 2.2$ years on original preparation. Almost half of individuals (35, 47.3%) were on concomitant immunosupressants and one patient had systemic corticosteroids. Majority of patients, 52 (72.2%) were at the time of switch (week 0, W0) in clinical remission, 16 (22.2%) had mild to moderate active disease and 4 (5.6%) individuals had severe disease activity. Comparing W0 and W56, no significant difference in C-reactive protein levels ($4.3 \pm 8.0$ mg/L vs. $3.3 \pm 3.8$; $p = 0.89$) and FC ($135 \pm 153$ µg/g vs. $199 \pm 225$; $p = 0.17$) was observed. Likewise, no increase in immunogenicity was found (ATI positivity: 9.5% vs. 6.0%, $p = 0.54$). Furthermore, clinical disease activity was stable until the end of follow-up (remission at W0 vs. W24: 72.2% vs. 77.8%; median difference of both HBI and SCCAI between W0 and W56 was 0). We found statistically significant increase in IFX TL ($3.4 \pm 3.8$ µg/mL vs. $4.7 \pm 4.5$, $p = 0.01$) which was by further ANOVA analysis explained by larger share of patients with intensified therapy at W56 (13.5% vs. 26.9%). Six patients discontinued IFX treatment up to W56 due to loss of response ($n = 2$ UC patients), adverse event ($n = 2$) and gravidity ($n = 2$). No patient experienced infusion reaction and the frequency and type of adverse events were similar to those observed during treatment with original IFX.

**Conclusion:** Based on our results switching of IBD patients from original to biosimilar IFX is effective and safe. Importantly, no increase in immunogenicity was observed.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1411 THE EVOLUTION OF INDICATIONS AND OUTCOMES OF SURGERY FOR PATIENTS WITH CROHN'S DISEASE DURING THE BIOLOGICAL AGENT ERA

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**Introduction:** Inflammatory bowel disease is common, affecting 61,000 Australians and costing approximately $2.7 billion per annum. Studies are equivocal on the affects of biological agents on the primary indication of surgery.

**Aims & Methods:** To determine if the introduction of biological agents has changed the indications and outcomes of surgery for patients with Crohn's disease. In accordance with the theorized mechanism of action of biological agents, it was hypothesized that there would be a reduction in penetrating disease with a concomitant rise in stricturing disease as the primary indication of surgery. From 1996 to 2013, sequential surgical procedures performed on patients with Crohn's disease at two large West Australian metropolitan hospitals were recorded. The cohort was divided into pre- biological agent [pre-BA] availability (1996–2006) and post-biological agent [post-BA] availability (2007–2013). The difference in the frequency of indications for surgical procedures and outcomes between the cohorts was determined statistically using chi-square tests.

**Results:** 224 patients underwent 244 surgical procedures (pre-BA, $n = 105$; post-BA, $n = 139$). The mean age was 40.6 years with a larger percentage of females in pre-BA (66.7%) than post-BA (47.5%; $\chi2\ (1) = 8.92$, $p = 0.003$). There was no change in the primary indication for surgery. Rates of emergency surgery decreased from 19% to 8.6% ($\chi2\ (1) = 5.69$, $p = 0.017$). Patients requiring a stoma decreased from 30.5% to 15.8% ($\chi2\ (1) = 7.45$, $p = 0.008$). There was a significant difference in the number and types of anastomoses between groups.

**Conclusion:** There was no clear evidence that the introduction of biological agents changed the indications for surgery in this cohort. The study does demonstrate a reduction in emergency surgeries and stomas, leading to better overall patient outcomes. Further investigation of individual patient response to biological agents is warranted.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1412 DETERMINATION OF LOWER ADALIMUMAB CUT-OFF LEVELS IN PATIENTS WITH CROHN'S DISEASE

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**Introduction:** Adalimumab (ADA) is a well-documented, effective and safe treatment option for moderate to severe Crohn's disease (CD). The drug is administered and dosed in a standard treatment regimen, but serum drug concentration (SDC) measurements offer the possibility to optimize the treatment strategy. However, an optimal therapeutic SDC range should be established to avoid the risk of adverse effects from too high - or suboptimal effect due to too low SDCs.

**Aims & Methods:** Our aim was to determine the lower cut-off of the therapeutic serum concentration (TSC) in a cohort of CD patients, who had received three or more doses of ADA, using CRP as a marker of inflammation and disease activity. In a subgroup analysis of a cross-sectional study at Stavanger University Hospital on IBD patients treated with anti-TNF-a agents, we identified adult patients with CD who were treated with ADA. Treatment interval and duration, drug dosage, time since onset of disease, CRP, SDC, age and gender were recorded. SDCs were measured using an in-house assay automated on the AutoDELFIA immunoassay platform at Oslo University Hospital, Radiumhospitalet. A CRP above 10 mg/L was chosen as a surrogate marker for significant inflammation and active disease, 10 (9.9%) of the included patients fulfilled this criterion. In total, 103 patients were included, of which 101 (98%) had a valid SDC.

**Results:** Median (range) age was 35 (16–78) years, and 47.5% were men. Median duration of treatment was 32 (2–110) months, with median time since onset of disease 9 (1–36) years. Median ADA dosage was 40 (40–80) mg, and median treatment interval 2 (1–2) weeks. Median SDC was 6.9 (0–24.6) mg/L. Median CRP was 2.8 (1–45) mg/L. Seven (6.9%) of the patients presented with anti-drug antibodies. A receiver operating characteristics (ROC) analysis gave an area under the curve of 0.743 (std. error 0.076, $p = 0.012$, 95% CI 0.595–0.891). An optimal cut-off of TSC in terms of optimizing sensitivity and specificity was found at 5.55 mg/L, with a sensitivity of 70% and a specificity of 69.2%. Thirty-four (33.7%) patients had a SDC below this threshold.

**Conclusion:** A lower therapeutic cut-off concentration of 5.55 mg/L was identified for Crohn's disease patients under established treatment with adalimumab, using CRP as marker for active disease. Identifying this value may help optimize the ADA treatment for CD patients, and avoid insufficient serum concentration levels with subsequent increased inflammatory activity.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1413 ANTI-TNF THERAPY IN REFRACTORY POUCHITIS AND CROHN'S DISEASE-RELATED COMPLICATIONS OF THE POUCH AFTER ILEAL POUCH-ANAL ANASTOMOSIS FOLLOWING COLECTOMY FOR ULCERATIVE COLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** Pouchitis is the most common complication after ileal pouch-anal anastomosis following colectomy for ulcerative colitis. Approximately 15% of the patients experienced chronic pouchitis refractory to antibiotics. In the last decade, it has been well established, that a secondary Crohn's disease–associated pouch complication could also occur in these patients. Data about the effectiveness of anti-TNF agents in refractory pouchitis or Crohn's disease–associated pouch complications remains sparse and the definitions of these two entities often overlap in the available articles.

**Aims & Methods:** We aimed to perform a systematic review and meta-analysis to evaluate the efficacy of anti-TNF therapy in differentiating patients with

chronic refractory pouchitis and CD-related complications. To identify relevant articles and abstracts, a systematic literature search was performed using both medical subject headings (MESH) and keywords (restricted to English language) and was performed in MEDLINE (1966 to December 2015). Abstracts of international congresses (DDW, UEGW, ECCO) were inspected by a manual search. The search process, selection of the manuscripts, and data extraction were performed independently by two physicians, and discrepancies between them were resolved by a third physician. Our work was performed according to the PRISMA statement. Statistical analysis was conducted using Comprehensive Meta-analysis software and Stata software. Prevalence and 95% confidence interval were estimated using random-effects models assuming between and within study variability. Statistical heterogeneity between results was assessed by examining forest plots, confidence intervals and using $I^2$. A sensitivity analysis was conducted to assess the influence on the global prevalence of the inclusion and exclusion of studies. CD-related complications of the pouch were defined as the presence of non-anastomotic fistula and/or non-anastomotic stenosis and/or prepouch ileitis. Chronic refractory pouchitis was defined as inflammation limited to the pouch. Inflammatory complications of the pouch included the two former entities.

**Results:** We identified a total of 21 articles and 3 abstracts, most of these retrospective case series, including a total of 313 patients treated either with infliximab (n = 232) or adalimumab (n = 81) (Table 1).

Main characteristics of the 24 studies included in the meta-analysis

| Studies | Nb of patients | Type of anti-TNF | Concomitant IS | Short term complete response | Long term complete response | Quality of the study (SIGN criteria) |
|---|---|---|---|---|---|---|
| **Kelly et al. 2016** | **42** | **IFX** | **26%** | **48%** | **29.6%** | **2++** |
| **Uchino et al. 2015** | **10** | **IFX** | **10%** | **40%** | **40%** | 2++ |
| Robbins et al. 2015 | 25 | ADA | NA | NA | 72% | 2+ |
| Ilzuka et al. 2014 | 1 | IFX | 0% | 0% | 100% | 3 |
| Viazis et al. 2013 | 7 | IFX | 71.4% | 71.4% | 85.7% | 2++ |
| Barreiro-de-Acosta et al. 2012 | 33 | ADA | 54.5% | 21.2% | 27.3% | 2++ |
| Li et al. 2012 | 48 | ADA | 10.4% | 50% | 33.3% | 2++ |
| Barreiro-de-Acosta et al. 2012 | 8 | ADA | 37.5% | 12.5% | 25% | 2++ |
| Haveran et al. 2011 | 13 | ADA | 69.2% | NA | 53.8% | 2- |
| Yeates et al. 2010 | 1 | IFX | 100% | 0% | 100% | 3 |
| Ferrante et al. 2010 | 28 | IFX | 71.4% | 35.7% | 39.2% | 2++ |
| Gionchetti et al. 2010 | 12 | IFX | 0% | 75% | NA | 2++ |
| Gionchetti et al. 2010 | 7 | ADA | 0% | 71.4% | NA | 2++ |
| Akitate et al. 2009 | 1 | IFX | 0% | 0% | 100% | 3 |
| Calabrese et al. 2008 | 10 | IFX | 0% | 90% | 80% | 2+ |
| Shen et al. 2008 | 17 | ADA | 0% | 41.2% | 47.1% | 2++ |
| Molnar et al. 2008 | 1 | IFX | 0% | 100% | 100% | 3 |
| Coburn et al. 2006 | 1 | ADA | 100% | NA | 100% | 3 |
| Kooros et al. 2004 | 4 | IFX | 75% | 50% | 100% | 3 |
| Viscido et al. 2003 | 7 | IFX | 100% | 71.4% | 57.1% | 2++ |
| Colombel et al. 2003 | 26 | IFX | 92.3% | 61.5% | 29.2% | 2+ |
| Huang et al. 2003 | 2 | IFX | 100% | 100% | 100% | 3 |
| Arnott et al. 2001 | 2 | IFX | 0% | 0% | 0% | 3 |
| Ricart et al. 1999 | 7 | IFX | 85.7% | 85.7% | 71.4% | 2+ |

The short-term and the long-term responses were evaluated at 8 weeks 95%CI [5–10] and 12 months 95%CI [12–18.5], respectively. Overall, the rate of complete response after anti-TNF induction therapy for inflammatory complications of the pouch was 0.51 (95%CI [0.39–0.64]; $I^2 = 0.56$). The rate of short-term complete response was 0.57 (95%CI [0.38–0.75]; $I^2 = 0.36$) for infliximab-treated patients compared to 0.38 (95%CI [0.08–0.72]; $I^2 = 0.50$) for adalimumab-treated patients (p = 0.20). The long-term rate of complete response in patients treated with anti-TNF therapy was 0.52 (95%CI [0.39–0.65]; $I^2 = 0.59$), with 0.59 (95%CI [0.45–0.72]; $I^2 = 0.30$) for infliximab-treated patients compared to 0.30 (95%CI [0.15–0.46]; $I^2 = 0.00$) for adalimumab-treated patients (p = 0.19). Considering only the patients for those data are sufficient to differentiate refractory pouchitis from Crohn's disease-related complications of the pouch (n = 210), the rate of complete response after anti-TNF induction therapy for inflammatory complications of the pouch was 0.52 (95%CI [0.36–0.68]; $I^2 = 0.56$). The rate of complete response after anti-TNF induction therapy seemed to be higher for Crohn's disease-related complications of the pouch 0.64 (95%CI [0.5–0.77]; $I^2 = 0.18$), compared to refractory pouchitis 0.10 (95%CI [0.08–0.35]; $I^2 = 0.00$) (p = 0.06). The rate of long-term complete response in patients treated with anti-TNF was 0.57 (95%CI [0.43–0.71]; $I^2 = 0.32$) for Crohn's disease-related complications of the pouch compared to refractory pouchitis 0.37 (95%CI [0.14–0.62]; $I^2 = 0.47$) (p = 0.57).

**Conclusion:** Despite wide heterogeneity of the data, anti-TNF agents have a clear trend to have higher and faster efficacy in Crohn's disease-related complications of the pouch compared to refractory pouchitis, highlighting the need to differentiate these two entities in clinical practice.

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All other authors have declared no conflicts of interest.

## P1414 PSYCHO-SOCIAL PREDICTORS FOR NONCOMPLIANCE TO CHRONIC DRUG TREATMENT IN CROHN'S DISEASE

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**Introduction:** Crohn's disease is a chronic condition requiring maintenance therapy to prevent relapse and further complications. Adherence to therapy and compliance with treatment is associated with improved outcomes.

**Aims & Methods:** We aimed to identify psycho-social and other risk factors associated with noncompliance to chronic drug treatment in Crohn's disease. Methods: A total of 128 outpatients attending the gastroenterology clinics in Soroka Medical Center and diagnosed with Crohn's disease, on maintenance treatment for a period of one year (6 month before and after study enrollment), were eligible for this study. Patients completed questionnaires including demographics, disease activity using the Harvey Bradshaw Index (HBI), psychological data including the Brief Symptom Inventory (BSI) and COPE questioners and the SF-36 & SIBDQ questionnaires regarding Health Related Quality of Life (HRQoL). For each patient, drug refill information for the study period was obtained from computerized pharmacy records. Compliance was defined as at least 80% acquisition of prescribed medication. Univariate analysis and regression models were used to identify significant associations for compliance as a continuous or a dichotomic variable.

**Results:** Of 128 patients 78 (61%) were noncompliant with maintenance treatment. Noncompliant patients were more likely to be unemployed (47.4% vs. 28.6%, p = 0.035), associated with "poor" economic status (30.3% vs. 8.5%, p = 0.004), with active Crohn's disease (54.2% vs. 27.9%, p = 0.006), lower SIBDQ score (median 44(IQR 9,68) vs. 52.5(20.70), p = 0.004), higher psychologic distress GSI score (0.42(0,2.39) vs. 0.23(0,1.68), p = 0.009), and lower SF 36 - Physical Functioning sub-scale (44.14(14.09,65.91) vs. 46.74(25.73,60.13), p = 0.03). Coping strategies were not related to compliance. We performed a quantile regression model, to better understand the differential effect of the variables along different quantiles of compliance. We found that disease duration (B = -0.026, p < 0.001, 95% CI -0.031–0.02), and higher number of Crohn's medications (B = -0.217, p = 0.004, 95% CI -0.365–0.07) were consistent predictors for low compliance in the lower quantiles (0–40% compliance), and "poor" economic status (B = -0.148, p = 0.004, 95% CI -0.248–0.048) as a predictor in the higher quantile (80% compliance).

**Conclusion:** Noncompliance is associated with unemployment, "poor" economic status, low quality of life score, high psychological distress, and lower SF 36 - Physical Functioning sub-scale. In multivariate regression analysis the strongest effect on noncompliance is derived from increasing medication number. These patient characteristics may be helpful in targeting those patients with higher risk for noncompliance.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1415 PATTERNS OF ADALIMUMAB USE AND ASSOCIATED COSTS IN INFLAMMATORY BOWEL DISEASE PATIENTS: AN ANALYSIS OF REAL-WORLD HEALTH CLAIMS DATA IN THE NETHERLANDS

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**Introduction:** An increasing number of inflammatory bowel disease (IBD) patients receive treatment with adalimumab. Patterns of adalimumab use and associated costs have never been described in a large real-life cohort. The aim of this study was to investigate patterns of adalimumab use and drug survival in a large real-life cohort of IBD patients.

**Aims & Methods:** We analyzed health insurance claims data of Achmea, the largest health insurance provider in the Netherlands, with a population of approximately 4 million insured persons. Data on healthcare use of adult IBD patients and prescription drugs were collected from 2008 to 2014. Drug survival was evaluated using Kaplan-Meier analysis in patients starting with adalimumab treatment who were insured by Achmea during the entire observation period.

**Results:** In this cohort, the number of patients who received IBD-related care ranged from 8695 in 2008 to 11065 in 2014. Cohort characteristics are provided in table 1. A total of 1496 IBD patients were treated with adalimumab during the

observed period. The annual proportion of IBD patients that received at least one prescription of ADA increased from 2.8% in 2008 to 8.1% 2014. When only drug costs are considered, annual costs of ADA treatment increased from €3,155,702 in 2008 to €13,006,126 in 2014. Since 2008, 1401 patients started with adalimumab. Drug survival was evaluated in 875 patients (77% Crohn's disease). Median drug survival of all patients was 648 days (95% CI 550–746). Crohn's disease patients were treated significantly longer than ulcerative colitis patients with a median drug survival of 727 and 390 days respectively ($p = 0.011$). No association was found between drug survival and gender ($p = 0.08$). Respectively 6 months, 1 year and 2 years after the initiation of treatment, 65%, 48% and 30% of patients were still receiving adalimumab.

**Table 1:** Cohort characteristics.

| Patients receiving IBD care | 2008<br>8695 | 2014<br>11065 |
|---|---|---|
| - Crohn's disease (n,%) | 3926 (45%) | 5070 (46%) |
| - male gender (n,%) | 3953 (45%) | 4926 (45%) |
| IBD patients receiving adalimumab | 246 | 892 |
| - Crohn's disease (n,%) | 221 (90%) | 716 (80%) |
| - male gender (n,%) | 83 (34%) | 382 (43%) |
| - combination treatment (n,%) | 74 (30%) | 270 (30%) |
| Adalimumab costs | €3,155,702 | €13,006,126 |

**Conclusion:** Adalimumab use and associated costs increased from €3,155,702 in 2008 to €13,006,126 in 2014. The majority of adalimumab discontinuation occurs within 1 year after initiation. Crohn's disease patients are treated significantly longer with adalimumab than ulcerative colitis patients.

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G.R.A.M. D'Haens: Not enough space to disclose all possible conflicts of interest. Please contact author if necessary.
M. Löwenberg: M. Löwenberg has served as speaker or principal investigator for Abbvie, Covidien, Dr. Falk, Ferring, Merck Sharp & Dohme, Receptos, Takeda, Tillotts and Tramedico. He has received research grants from AbbVie, MSD, Achmea healthcare and ZonMW.
All other authors have declared no conflicts of interest.

## P1416 SYSTEMATIC LITERATURE REVIEW ON THE IMMUNOGENICITY OF BIOLOGICS IN INFLAMMATORY BOWEL DISEASE

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**Introduction:** Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory disorders that can be treated with biologic therapies. While the development of such therapies has led to key improvements in the treatment of IBD for the last decade, a loss of efficacy over time is often observed with biologic therapies, with immunogenicity a leading contributor to this loss of response.

**Aims & Methods:** The objective of this analysis was to evaluate evidence on the formation of anti-drug antibodies (ADAbs) to biologics used to treat IBD. A systematic literature review was conducted focusing on adalimumab (ADM), certolizumab pegol (CZP), golimumab (GLM), infliximab (IFX), ustekinumab (UST) and vedolizumab (VDM). Online searches included MEDLINE®, Embase® and the Cochrane Central Trials Register for the period from January 2009 to August 2015. Key congresses and references in selected articles were hand-searched. Eligible studies involved patients with CD or UC, and were randomised controlled trials (RCTs), non-RCTs or observational studies. Case reports/series/studies, systematic/literature reviews, letters, commentaries and editorials were excluded. Abstracts identified were screened for eligibility by one reviewer, with a second reviewer checking 10% of screened abstracts. Articles considered eligible were subject to full-text review. Study quality was assessed using recognised quality assessment tools (including the Jadad scoring system) and studies with a high risk of bias were excluded.

**Results:** A total of 22,334 abstracts were screened; 938 articles were retrieved for full-text review and 114 studies from 122 publications assessed. Of these, 5 studies were excluded due to high risk of bias. Over 90% of studies reported on IFX and ADM, reflecting the time these agents have been on the market (Table 1). Few studies were available for the more recently approved agents CZP ($n = 4$), GLM ($n = 2$), UST ($n = 1$) and VDM ($n = 4$). IFX was the most immunogenic agent (based on 10 RCTs and 63 non-RCTs or observational studies) and UST the least (based on 1 RCT) (Table). Immunogenicity was measured at differing time points dependent on dosing intervals and local protocols. ADAbs were detected as early as 10–14 days post-dosing but can take months to develop. An association was found between reduced efficacy of ADM and IFX therapy and the presence of ADAbs. For ADM, the presence of ADAbs did not correlate with safety, but more ADAb-positive patients receiving IFX reported AEs than ADAb-negative patients. For ADM, CZP and IFX, ADAb-positive patients had lower serum levels of the biologic than ADAb-negative patients. One study reported monitoring ADAbs to IFX in CD was more cost effective than dose escalation without drug monitoring and immunogenicity assessment.

**Table:** Range of rates of ADAbs formation to biologics in patients with CD or UCab

| Biologic agent | All studies | CD (n) | UC (n) | CD or UC (n) |
|---|---|---|---|---|
| Adalimumab | 0.3–38% (22) | 0.3–35% (11) | 2.9–5.3% (3) | 14–38% (8) |
| Certolizumab pegol | 3.3–25.3% (4) | 3.3–25.3% (4) | - | - |
| Golimumab | 0.4–2.9% (2) | - | 0.4–2.9% (2) | - |
| Infliximab[c] | 0–65.3% (73) | 2.9–60.8% (22) | 6.1–41% (8) | 0–65.3% (43) |
| Ustekinumab | 0.7% (1) | 0.7% (1) | - | - |
| Vedolizumab | 1–4.1% (4) | 1–4.1% (2) | 3.7% (1) | 4% (1) |

[a]Only studies reporting rates of ADAbs were included (8 studies did not report specific proportions of patients developing ADAbs).[b]Immunogenicity analyses are product- and assay-specific.[c]Selected studies excluded from analysis due to small sample size ($n = 28$) and high rates of immunogenicity.- Indicates no publications available.ADAbs, anti-drug antibodies; CD, Crohn's disease; UC, ulcerative colitis.

**Conclusion:** The potential clinical implication of lower biologic serum concentrations in the presence of immunogenicity is a concern for effective treatment and requires further study. In particular, more studies are required to assess the immunogenic potential of the more recently approved biologics. Diversity of study designs, patient populations, disease severity, concomitant therapies, assay methods and timing limits comparisons across studies. However, this analysis suggests that agents eliciting the lowest rate of immunogenicity may be preferential for treating CD and UC.

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## P1417 TREATMENT OF BONE MARROW MESENCHYMAL STROMAL CELLS REDUCES THE ACTIVITY ANKYLOSING SPONDYLITIS ASSOCIATED WITH CROHN'S DISEASE

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**Introduction:** Patients with ankylosing spondylitis (AS) and Crohn's disease (CD) should be administered early aggressive therapy, how effective in inflammatory bowel disease (IBD) and articular manifestations. Nonsteroidal anti-inflammatory drugs (NSAID) effective for the treatment of rheumatic manifestations, but their use is associated with an exacerbation of IBD. For the treatment of CD are also using mesenchymal stromal cells (MSCs). Also conduct safety studies and efficacy of MSCs for the treatment of AS. Objective: To compare the efficacy of therapy mesenchymal stromal cells (MSCs), bone marrow, and the standard anti-inflammatory therapy in the extra-intestinal manifestations (sacroiliitis and ankylosing spondylitis) in patients with Crohn's disease (CD).

**Aims & Methods:** 34 CD patients with extraintestinal manifestations (ankylosing spondylitis and sacroiliitis, are not related to the activity of Crohn's disease) were divided into two groups. The first group of patients aged 18 to 58 years (Me-34) ($n = 16$) received MSCs culture scheme (0–1–2–3, then every 26 weeks). The second group of patients with CD ($n = 18$) aged 20 to 60 years old (Me-28) received standard anti-inflammatory therapy with glucocorticosteroids (GCS) and immunosuppressive (IS). Evaluation of efficacy was conducted on the level of activity of inflammation (CRP, thrombocytosis) and ankylosing spondylitis activity index (BASDAI) were performed at 12, 25 and 52 weeks of therapy.

**Results:** Among the patients in 1-st group reduction in the activity of the AS after 12 weeks of observation occurred in 4/16 patients (25.9%). In 2-nd group, a decrease in activity of the AS occurred in 5/18 (27.7%) ($p = 0.83$). After 26 weeks in patients (group 1) receiving MSCs, reducing the activity of the AS occurred in 10/16 (62.5%). In 2 group, a decrease in activity of the AS occurred in 5/18 (27.7%) ($p = 0.044$). After 52 weeks in 1 group patients the minimal activity of the AU persisted in 10/16 (62.5%) patients with CD. In 2 group, there was increased activity of the AS in one patient 4/18 (22.2%) ($p = 0.042$).

**Conclusion:** MSCs transplantation can reduce the activity of the AS associated with Crohn's disease compared to standard anti-inflammatory GCS/IS therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

1. Wang P, Li Y, Huang L, Yang J, Yang R, Deng W, Liang B, Dai L, Meng Q, Gao L, Chen X, Shen J, Tang Y, Zhang X, Hou J, Ye J, Chen K, Cai Z, Wu Y and Shen H. Effects and safety of allogenic mesenchymal stem cell intravenous infusion in active ankylosing spondylitis patients who failed NSAIDs: a 20-week clinical trial. *Cell Transplant* 2014; 23(10): 1293–303.

## P1418 BIOLOGICAL THERAPY AND PREGNANCY IN INFLAMATORY BOWEL DISEASE: THE LONG-TERM SAFETY OF IN UTERO EXPOSURE IN A TERCIARY CENTER

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**Introduction:** Inflammatory Bowel Disease (IBD) is often diagnosed in the reproductive age group. FDA classify the anti-TNF drugs as presumably safe in IBD, although the literature is scarce and focus mainly on the short-term effects.
**Aims & Methods:** We aimed to evaluate the long-term safety of in utero exposure to the anti-TNF drugs in IBD. Methods: Case-control retrospective study of all pregnancies in IBD, in a tertiary center between 1994–2015. It was compared 2 groups: with exposure (cases) and without exposure (controls) to the anti-TNF drugs up to 3 preconception months. The exclusion criteria include pregnancies with no sufficient data, scheduled abortion or pregnancies that occurred previously to IBD diagnosis. It was evaluated obstetric complications and fetal prognosis, including birth defects, serious infections (infections requiring hospitalization), allergies and tumors.
**Results:** It was included 59 pregnancies, corresponding to 35 IBD women with an average of $2.4 \pm 1.4$pregnancies. The average age of conception was $32.0 \pm 4.6$years. Most pregnant women had Crohn's disease (67.8%;n = 40). The anti-TNF exposure in pregnancy occurred in 11(18.6%) IBD women, of which 5(45.4%) in monotherapy. The proportion of complications during pregnancy (18.2%vs22.9%;p = 0.733), including the number of abortions (9.1%vs16.7%;p = 0.528), during delivery (30.0%vs37.5%;p = 0.659) and in newborn (20.0%vs20.0%;p = 1.000) were similar in both groups. For an average follow-up in post-delivery of $6.7 \pm 4.8$years ($2.5 \pm 2.0$vs$7.7 \pm 4.7$years;p = 0.001), there was a higher proportion of serious infections in newborns of anti-TNF-exposed mothers (40.0%vs7.5%;OR8.222;p = 0.008), without differences in length of stay ($2.2 \pm 0.5$vs$4.3 \pm 4.9$days;p = 0.425) or diagnosis age of infection ($1.0 \pm 0.6$vs$1.2 \pm 1.4$years;p = 0.816). None of infections required intensive care or resulted in sequelae. There were no significant differences in the development of allergies (0.0%vs15.0%;p = 0.192) or neoplasia (0.0%vs2.5%;p = 0.614). After multivariate analysis, the only factor associated with the occurrence of serious infections was intrauterine exposure to anti-TNF (OR9.867;p = 0.011).
**Conclusion:** Intrauterine exposure to anti-TNF seems to be associated with increased risk of serious infections, especially in the first post-delivery year, although with no long-term complications. Further large-scale investigations are necessary in order to evaluate the real impact of these drugs in the infectious risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1419 INFLAMMATORY CYTOKINES AND THEIR REGULATION OF 11 BETA HYDROXYSTEROID DEHYDROGENASE TYPE 2 IN IBD PATIENTS

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**Introduction:** Endogenous Glucocorticoid metabolism may represent a key regulatory pathway in IBD. 11-beta hydroxysteroid dehydrogenase type 2 (11BHSD-2) is a key isoenzyme which dehydrogenase, converting the active GC cortisol (corticosterone in rodents) to inactive cortisone. We have previously shown that decreased levels of 11 BHSD2 are found in IBD patients and are independent of the glucocorticoid receptor and other cofactors. Recognised regulators of 11BHSD2 include pro inflammatory cytokines often associated with inflammation. Their effect on 11BHSD 2 expression in IBD patients is unknown.
**Aims & Methods:** We aimed to determine the association between key pro inflammatory cytokines (IL-6, TNF$\alpha$, IL-1 Beta and Rela (subunit for NFKB)) and 11BHSD2 expression in an IBD cohort. **Method:** Following informed consent, patients with known IBD aged 18–80yrs were prospectively recruited; exclusion criteria: (1) Steroid $\leq$ 6weeks (2) Coagulopathy, (3) Pregnancy, (4) Cushing/Conns Syndrome. Disease activity was assessed using biochemical (CRP), clinical (Harvey-Bradshaw Index/Mayo Score), endoscopic & histological parameters. Controls with a normal colonoscopy without a history of IBD were also recruited. Biopsies were obtained from inflamed tissue from IBD patients and a single colonic biopsy was obtained from controls. Biopsies were stored in RNA later & analyzed in batch, using Quantitative real time RT-PCR (TaqMan) & commercially available Probes & Primers. Relative transcript levels were determined using 18 S as a reference gene. Relative expression of 11BHSD2, IL-6, TNF$\alpha$, IL-1Beta and Rela (NFKB) were calculated as a mean and compared among groups using a student t test and subjects were controlled for for disease activity based on clinical, biochemical, histological and endoscopic parameters. A p value of $\leq 0.05$ was considered significant.
**Results:** To date 24 IBD patients (17 Ulcerative Colitis (UC) & 7 Crohn's Disease (CD)) and 12 controls have been recruited. IBD and control cohorts were demographically similar with 63% vs 58% being male with a mean age of 45yrs (range 20–67yrs) and 53yrs (range 25–83) respectively. Amongst the IBD cohort, 33% (n = 8) had severe, 46% (n = 11) moderate and 21% (n = 5) mild disease histologically. The mean HBI score and mayo was 7 (range 0–12 and 0–21 respectively) and the mean CRP was 35.4 mg/l (range 1–184.3 mg/l).Overall there was a significant downregulation of 11BHSD2 amongst IBD patients compared with controls, 11.06 au vs. 153 au, $p \leq 0.01$ 95%CI 30.9–252.9. Expectantly, levels of IL-1Beta, IL-6, TNF $\alpha$ and Rela were all significantly higher amongst IBD patients vs. controls as outlined in Table 1. They were also statistically upregulated in patients with more active disease as outlined in Table 1. This was accompanied by a downregulation of 11BHSD2, (active 4.8 vs inactive 12.1 au, $p \leq 0.1$), although it did not quite reach statistical significance.

**Table 1:** Relative expression of 11BHSD2 and cytokines overall & according to disease activity.

| Mean Relative Expression (au) | IBD Patients N = 24 | Controls N = 12 | P value | Active patients N = 14 | Inactive patients N = 10 | P value |
|---|---|---|---|---|---|---|
| **11BHSD 2** | 11.06 | 153 | $\leq$0.01 | 4.8 | 12.1 | NS |
| **IL-6** | 18.2 | 0.6 | $\leq$0.02 | 25.5 | 5.2 | $\leq$0.03 |
| **TNF $\alpha$** | 6.0 | 1.3 | $\leq$0.02 | 7.9 | 2.6 | $\leq$0.04 |
| **IL-1Beta** | 13.1 | 0.2 | $\leq$0.02 | 17.9 | 5.3 | $\leq$0.04 |
| **Rela (NFKB)** | 3.1 | 1.0 | $\leq$0.03 | 4.0 | 1.6 | $\leq$0.05 |

**Conclusion:** Levels of 11BHSD 2 significantly lower in IBD patients in response to increased levels of key inflammatory cytokines during active inflammation. Dysregulation in this pathway could potentially explain exogenous GCS resistance and further work is warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1420 A CLINICAL TRIAL OF THE EFFECTS OF VAGUS NERVE STIMULATION IN BIOLOGIC-REFRACTORY CROHN'S DISEASE

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**Introduction:** The autonomic nervous system regulates innate and adaptive immunity (Andersson, *J Exp Med* 2012; 209:1057). Activation of its efferent arm, the Cholinergic Anti-inflammatory Pathway (CAP) by electrical vagus nerve stimulation (VNS) reduces inflammation and ameliorates disease in animal models of colitis (Matteoli, *Gut* 2013; 62:1214). VNS has been studied in a biologic-naïve Crohn's disease (CD) population showing significant benefit (Bonaz, *Neurogastoenterology*, 2016; doi:10.1111).
**Aims & Methods:** We studied the efficacy of VNS in biologic–refractory CD patients in a clinical trial. This is an open label study of patients with active CD (CDAI 220–450, stool calprotectin 200 µg/g, and SES-CD ulcer score $\geq$ 2 in at least 1 segment with centrally blinded endoscopy reading). Patients refractory to biologic agents (TNF antagonists and/or vedolizumab) entered an 8 week wash out. A VNS stimulation device was implanted, consisting of a pulse generator and an electrical lead tunneled into the carotid sheath and affixed to the vagus nerve. Two weeks following implantation stimulation was initiated (pulse width 250 microseconds, 10 Hz frequency, output current incremented by tolerability to a max of 2.0 mA, for 60 seconds). From 4 to 6 weeks the output current was increased and stimulation was increased to 5 minutes. At 8 weeks, stimulations were increased from QD to QID if CDAI remission was not achieved. The stimulation remained at this level from 8 to 16 weeks, the time point of repeat endoscopy and primary endpoint (PE).
**Results:** So far, 5/8 patients reached the PE (6 males, 38 years [range 21–65]). The median (IQR) CDAI decreased from 300 (271–388) to 171 (127–395), fecal calprotectin from 4708 (1996–9390) to 1153 (509–3861) µg/g, the hs-CRP from 5.95 (2.64–8.10) to 2.78 (1.45–7.13) mg/dL and the SES-CD from 24.5 (17.1–29.0) to 19.0 (13.5–28.5). There were 3/5 patients with CDAI-100 response, 2/5 with CDAI remission, and 4/5 with reduced SES-CD. There were 9 Serious Adverse Events occurring in 5/8 patients, all of which were CD-related except for 1 (device-related postoperative infection).
**Conclusion:** VNS induced clinical and endoscopic improvement in a significant proportion of highly refractory CD patients. The trial is ongoing and additional patients will be studied.
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## P1421 PREDICTORS OF THE RESPONSE TO CORTICOSTEROIDS TREATMENT IN THE ULCERATIVE COLITIS

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**Introduction:** Ulcerative colitis (UC) may require corticosteroid treatment [1], without a reliable predictable index of response [2], except in patients with severe UC by means of Ho risk score [3], to facilitate second-line treatment or surgery [1].

**Aims & Methods:** The aims of the study were: - To assess whether the predictive value of Ho index might be applied to identify no responding patients to corticosteroid treatment in all cases of UC, independently of the severity of the disease. - To search for predictors of corticosteroids efficiency in patients with UC based on clinical characteristics and biological markers of the patients. For these, an observational retrospective study of 14 years, including 136 patients of both sexes, analyzing epidemiological and sociodemographic characteristic and clinical parameters regarding their response to corticosteroids in different phases was performed.

**Results:** UC debuts at any age, although in our sample there are three peaks: at 31, 47 and 69 years, without gender differences [4]. The 20.59% of the patients were never treated with corticosteroids, which mostly correspond to A3 and / or E1 and / or S0–1 of Montreal Classification [1]. The patients treated with corticosteroids, depending on their response, were divided in: no responding (33.09%), corticosteroid dependent (24.26%) or corticosteroid refractory (8.82%), and good responding UC (46.32%) (4). In the good responding patients the efficacy to corticosteroids decreased linearly after successive treatments (X), fitting to an equation: $Y_{\text{Percent responding}} = -13.53 + 92.38 * X$, with 98.9% of predictive response. Ho index, validated in severe UC [3], might only have a predictive value in cases with low score (0–1 points) and in the first administration of corticosteroids. But not for the remaining cases of UC. The binary logistic regression analysis gave a predictive model of response (in 75.7% of cases) to the first corticosteroid treatment, taking into account the age of the patients at diagnosis (years), the days delayed before initiation of treatment after the diagnosis of UC, and the C-Reactive Protein (CRP) (mg/l). The equation was: $Y_{\text{Responding (yes/no)}} = -1.5717 + \text{age} * 0.045 + \text{days delayed initiation treatment} * 0.0007 - \text{CRP} * 0.0105$.

**Conclusion:** - In patients responding to corticosteroids treatment in the first administration the percentage of response successive treatments is linearly predicted. - Ho score risk lack of predictive value when applied to all cases of UC. - The analysis of binary logistic regression gave a predictive equation of response to corticosteroids based on the age of diagnosis of UC, number of days until the start of corticoid treatment and the value of CRP. This should be validated in a new sample of patients.

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## P1422 NUDT15 R139C GENOTYPE IS A DETERMINANT OF THIOPURINE-INDUCED LEUKOPENIA IN CHINESE PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A MUTI-CENTER ANALYSIS

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**Introduction:** The incidence of thiopurine-induced leukopenia is higher in Asians than in individuals of European descent, but the predictability based on TPMT genotype is limited, especially in Asian patients. NUDT15 R139C was firstly found to be associated with thiopurine-induced leukopenia in a Korean inflammatory bowel disease (IBD) cohort, which is not clear in Chinese population.

**Aims & Methods:** The aim of this study was to confirm the role ofNUDT15R139C genotypeson thiopurine-induced leukopenia in Chinese IBD patients and investigate the relevant factors. A multi-center study was conducted in four tertiary hospitals in different areas of China. IBD patients onstandard dose ofthiopurine-were recruited. Clinical and epidemiological characteristics were collected from IBD databases of each included center. NUDT15 R139C genotypeswere determined with PCR-RFLP and sequencing. The interactions between gene variant and leukopenia (white blood cell $< 3000\,mm^{-3}$) were analyzed. Logistic analysis was conducted to find the risk factors for leukopenia.

**Results:** A total of 758 patients were included. Among them, 107 (14.1%) patients developed leukopenia. There was significant association of NUDT15 R139C variant and thiopurine-induced leukopenia ($P = 7.24*10^{-21}$). All of the 11 homozygous variant carriers developed early leukopenia (<8 weeks), 31.7% (52/164) heterozygous carriers developed leukopenia, while only 7.9% (44/557) wild type carriers developed leukopenia. Compared with the wide type homozygotes (CC), patients carrying variant allele T (CT+TT) have much higher risk for leukopenia ($P = 7.63*10^{-7}$, OR = 4.97, 95%CI 2.63~9.39).The sensitivity, specificity, PPV and NPV of T allele for leukopenia were 43.5%,90.5%,39.7% and 91.7%. Significant higher risks for leukopenia were found in different stages (<8Ws, 8–24Ws and >24Ws) with different OR values. Multi-factor analysis found that female and NUDT15 R139C variant were independent risk factors for thiopurine-induced leukopenia. For heterozygous carriers, the available dosage was lower than the wild type ($P < 0.001$). The results were consistant in the included centers.

**Conclusion:** NUDT15 R139C could be a promising biomarker for thiopurine-induced leukopenia in Chinese patients with IBD and be helpful for individualized therapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1423 EFFECTS OF HIGH- AND LOW-FAT MEALS ON THE PHARMACOKINETICS OF OZANIMOD, A NOVEL SPHINGOSINE 1-PHOSPHATE RECEPTOR MODULATOR

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**Introduction:** Ozanimod (RPC1063) is an oral, selective sphingosine 1-phosphate (S1P) 1 and 5 receptor modulator in clinical development for the treatment of relapsing multiple sclerosis and inflammatory bowel disease. Since food has the potential to significantly influence the rate and extent of drug absorption, we designed and conducted a food-effect study with ozanimod.

**Aims & Methods:** The objective of this study was to characterize the effects of high-fat and low-fat meals on the pharmacokinetics (PK) of a single oral dose of ozanimod in healthy adult subjects. This was a randomized, open-label, 3-period, 6-sequence, crossover study. Twenty-four healthy adult subjects were enrolled to receive a single 1-mg oral dose of ozanimod under 3 different conditions separated by washout periods of 7 days: fasted (treatment A), with a standard FDA high-fat meal (treatment B), and with a low-fat meal (treatment C). PK parameters for ozanimod and its two active metabolites (RP101988 [major] and RP101075 [minor]) were calculated. Point estimates and 90% confidence intervals (CIs) about the geometric mean ratio between treatments for maximum concentration ($C_{max}$) and overall exposure ($AUC_{0\text{-inf}}$ or $AUC_{0\text{-last}}$) were determined using linear mixed-effects models.

**Results:** Twenty subjects completed both treatments A and B and 23 subjects completed both treatments A and C and provided PK data for the pair-wise comparison of fed vs fasted. The 90% CIs between fed (high-fat or low-fat) and fasted treatments for the $C_{max}$ and $AUC_{0\text{-inf}}$ of ozanimod and RP101988 were all within the no-effect boundary of 0.80 to 1.25. For the minor metabolite RP101075, the 90% CIs between high-fat and fasted for $AUC_{0\text{-last}}$ and the 90% CIs between low-fat and fasted for $C_{max}$ and $AUC_{0\text{-last}}$ were within the no-effect boundary. While the 90% CI between high-fat and fasted treatments for RP101075 $C_{max}$ (0.76 to 0.88) fell outside the lower bound of the no-effect boundary, this decrease was not considered to be clinically meaningful. Median time to reach $C_{max}$ ($T_{max}$) for ozanimod was delayed following a high-fat meal (12 hours) compared to fasted and low-fat meal conditions (8 hours), but the range (6 to 12 hours) was the same. Mean elimination half-life ($t_{1/2}$) values for ozanimod and its active metabolites ranged from 17–21 hours and were similar across all 3 treatments. Overall, single oral doses of 1 mg ozanimod were considered generally well tolerated.

**Conclusion:** Ozanimod may be taken with or without food.

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J.P. Hartung: Jeffrey P. Hartung is a former employee of Celgene, Inc.
C. Tompkins: Cindy-ann Tompkins is an employee of Celgene, Inc.
P.A. Frohna: Paul A. Frohna is an employee of Celgene, Inc.

## P1424 INFLIXIMAB DOSE DOUBLING IS EFFECTIVE FOR OPTIMIZING TROUGH CONCENTRATIONS AND REGAINING CLINICAL RESPONSE IN PATIENTS WITH CROHN'S DISEASE

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**Introduction:** Loss of response to infliximab (IFX) in patients with Crohn's disease can be managed by treatment intensification. Dose escalation could be preferred over interval shortening because of convenience for the patient.

However, evidence supporting dose doubling in Crohn's disease is sparse and controversial.
**Aims & Methods:** The aim of this study was to retrospectively review the effect of IFX dose doubling (from 5 mg/kg to 10 mg/kg body weight) on clinical response (based on physician global assessment and evaluated at the time of the next infusion) in a cohort of 70 patients with Crohn's disease following a loss of clinical response during maintenance treatment. IFX was measured in four consecutive trough samples before (T-1 and T0) and after (T + 1 and T + 2) dose doubling, using an in-house developed ELISA. Trough concentrations (TC) and CRP are shown as median [IQR].
**Results:** Dose doubling was clinically successful in 81% (n = 57) of the patients. Seventy percent (n = 49) of the patients received double dose IFX following an unsuccessful infusion interval shortening, resulting in an 84% (n = 41) response rate. The success rate of dose doubling as a first treatment intensification strategy was similar (76%, n = 16). The overall TC just before the infusion of 10 mg/kg IFX (T0) was 1.7 μg/mL [0.3 – 4.3] and was significantly higher in responders, 2.0 μg/mL [0.9 – 4.3], compared to non-responders, 0.3 μg/mL, [0.3 – 1.3] (p = .04). Dose doubling significantly increased TC to 5.2 μg/mL [1.7 – 10.1] at T+1 (p < .0001). Clinical response was associated with significantly higher TC after dose doubling at T+1, 5.5 μg/mL [3.0 – 10.4], compared to non-responders, 0.5 μg/mL [0.3 – 1.3] (p = .004). ROC analysis indicated that a target T + 1 IFX TC of 1.5 μg/mL is already associated with clinical response (88% specificity, 77% sensitivity, AUROC 0.75, p < .01). IFX TC increased between T0 and T + 1 in 73% (n = 51) of patients and was associated with a response rate of 90% (n = 46). In 27% (n = 19) of the patients no increase in TC was observed, which was associated with a significantly lower response rate of 58% (n = 11) (p = .004). An IFX TC increase > 1 μg/mL predicts clinical response (73% specificity, 85% sensitivity, AUROC 0.76, p < .01). Clinical response to dose doubling was also reflected in a significant decrease and normalization of CRP from 7.9 mg/L [1.7 – 22.4] at T0 to 4.4 mg/L [1.8 – 12.0] at T + 1 (p = .002), which did not occur in case of non-response (from 10.5 mg/L [3.9 – 62.5] to 5.1 mg/L [3.0 – 41.7]) (p = .5). CRP at T0 was not associated with response. Eight out of 13 non-responders received a second IFX infusion at 10 mg/kg at T + 1 which resulted in higher TC before the next infusion at T + 2 (6.0 μg/mL versus 0.7 μg/mL) but clinical response was never regained.
**Conclusion:** Dose doubling of IFX successfully restored the clinical response even when earlier infusion interval shortening attempts failed. During loss of response, IFX TC were sub-therapeutic (< 3 μg/mL), despite earlier infusion interval shortening attempts to regain response. Dose doubling was effective for restoring therapeutic IFX TC. Clinical response to IFX dose doubling is associated with higher pre- and post-escalation TC and with a normalization of CRP.
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All other authors have declared no conflicts of interest.

## P1425 ADD-ON THERAPY FOR INDUCTION OF REMISSION IN MILD-TO-MODERATE ULCERATIVE COLITIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** We performed a systematic review and meta-analysis to assess efficacy and safety of interventions used as adjunct to standard treatment in patients with active mild to moderate ulcerative colitis (UC).
**Aims & Methods:** Medline, Embase, Cochrane Central Register of Controlled Trials and reference lists of relevant reviews were systematically searched up to September 2015. We included randomised controlled trials of therapies added to current treatment with 5-aminosalicylic acid, immunosuppressants or steroids in patients with active UC. We synthesised results regarding remission, response, mucosal healing, and incidence of any adverse event. We quantified heterogeneity with the $I^2$ statistic.
**Results:** Seventeen studies (1338 patients) assessed efficacy of 6 adjunctive interventions. All studies were placebo controlled, except for one that compared beclomethasone propionate (BDP) with prednisone. Budesonide multimatrix (MMX), BDP, per os LMWH (Low Molecular Weight Heparin), transdermal nicotine and phosphatidylcholine all led to higher remission compared to placebo. Nevertheless, only per os (LMWH), transdermal nicotine, phosphatidylcholine and probiotics led to response, whereas mucosal healing was observed only following treatment with budesonide MMX or probiotics. Finally, all interventions but nicotine were associated with similar risk for any adverse event compared to placebo (table 1).
**Conclusion:** Budesonide MMX, BDP, phosphatidylcholine, probiotics and per os LMWH seem to be a safe option for adjunctive treatment of active mild to moderate UC. However, these conclusions are based on limited evidence, hence there is need for additional large trials.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1426 EFFICACY OF INFLIXIMAB BIOSIMILAR CT-P13 INDUCTION THERAPY ON MUCOSAL HEALING IN ULCERATIVE COLITIS

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**P1425 Table 1:** Results for efficacy and safety outcomes for adjunctive treatment of active mild to moderate ulcerative colitis compared to placebo. Significant changes are highlighted in bold.

| | **Remission** | | **Response** | |
|---|---|---|---|---|
| **Interventions (vs placebo)** | **No studies /No Patients** | **RR 95%CI)** | **No studies /No Patients** | **RR(95%CI)** |
| Budesonide MMX | 2/490 | **1.64(1.02–2.64)** | - | - |
| BDP | 1/119 | **1.70(1.13–2.56)** | 1/119 | 1.05(0.47–2.34) |
| BDP (vs prednisone) | 1/277 | 0.85(0.53–1.36) | 1/277 | 0.98(0.82 - 1.18) |
| LMWH p.o. | 1/135 | **1.35 (1.07–1.70)** | 1/135 | **1.24 (1.04, 1.48)** |
| LMWH sc | 1/100 | 1.08 (0.29 - 4.09) | 2/129 | 0.95 (0.70, 1.29) |
| Transdermal Nicotine | 2/136 | **2.09(1.09–3.99)** | 1/64 | **4.26(1.33–13.67)** |
| Phosphatidylcholine | 3/195 | **2.92 (1.69–5.05)** | 3/195 | 3.27 (0.85–12.69) |
| Probiotics-Bifidobacterium | 2/75 | 1.24(0.75–2.04) | 3/91 | **1.49(1.01–2.18)** |
| Probiotics-VSL#3 | 2/291 | 1.88(0.96–3.67) | 2/291 | **1.94(1.00–3.79)** |
| | **Mucosal Healing** | | **Any Adverse Event** | |
| | **No studies /No Patients** | **RR (95%CI)** | **No studies /No Patients** | **RR (95%CI)** |
| Budesonide MMX | 1/458 | **2.07(1.29–3.33)** | 1/458 | 1.17 (0.88, 1.55) |
| BDP | 1/119 | 1.89 (0.95–3.75) | 1/119 | 0.53 (0.10, 2.76) |
| BDP (vs prednisone) | 1/277 | 1.05 (0.68–1.63) | 1/282 | 0.78 (0.64, 0.94) |
| LMWH p.o. | 1/135 | 1.30 (0.65–2.63) | 1/141 | 0.94(0.58–1.53) |
| LMWH sc | - | - | 2/129 | 1.2 (0.92–1.57) |
| Transdermal Nicotine | 1/64 | 7.44(0.4–138.4) | 2/136 | **2.38 (1.61–3.51)** |
| Phosphatidylcholine | 2/135 | 4.27(0.19–97.30) | 2/134 | 1.02 (0.76–1.38) |
| Probiotics-Bifidobacterium | 1/56 | 1.75(0.58–5.32) | 2/75 | 3.00 (0.13–70.64) |
| Probiotics –VSL#3 | 1/147 | **2.18(1.12–4.23)** | 1/144 | 0.91 (0.37–2.24) |

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**Introduction:** CT-P13 is the first biosimilar to infliximab that was approved for the same indications as its originator infliximab. No data is available on the effect of infliximab biosimilar on mucosal healing.
**Aims & Methods:** The aim of this study was to evaluate the efficacy of CT-P13 induction therapy on mucosal healing in patients with ulcerative colitis (UC). UC patients, who received CT-P13 therapy from its local introduction at three Hungarian and one Czech IBD centres, were prospectively enrolled. Sigmoidoscopy was performed after the end of the induction therapy at week 14. Mucosal healing was defined as Mayo endoscopic subscore 0 or 1. Complete mucosal healing was defined as Mayo endoscopic subscore 0. Trough level of CT-P13 was measured at week 14.
**Results:** Sixty-three UC patients who underwent CT-P13 induction therapy were enrolled in the study. Indication of the therapy was acute, severe flare up and chronic, refractory activity in 24 and 39 patients. Cumulative clinical response and steroid-free remission at week 14 were achieved in 82.5% and 47.6% of the patients. Sigmoidoscopy revealed steroid-free mucosal healing in 47.6% of the patients, complete mucosal healing was present in 27%. Mayo endoscopic subscore decreased significantly at week 14 compared to baseline. Trough levels of infliximab correlated with mucosal healing.
**Conclusion:** This was the first study examining the efficacy of CT-P13 induction therapy on mucosal healing in UC. Our results indicate that mucosal healing is achieved in two thirds of UC patients by the end of the induction treatment with CT-P13.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1427 SUBTHERAPEUTIC LEVELS OF INFLIXIMAB AND ADALIMUMAB ARE ASSOCIATED WITH INCREASED DISEASE ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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**Introduction:** Anti-TNF-$\alpha$ agents have a central role in the treatment of moderate to severe inflammatory bowel disease (IBD), but low serum drug concentrations (SDC) may result in lack of response. Measuring SDC offers the possibility of individualized and optimized treatment.
**Aims & Methods:** Our aim was to determine the prevalence of subtherapeutic SDC in a cohort of IBD patients, who had received at least three doses of infliximab (IFX) or adalimumab (ADA). We also wanted to investigate whether SDC below our defined therapeutic ranges were associated with increased levels of disease activity markers. In a cross-sectional study at Stavanger University Hospital we included patients with ulcerative colitis (UC) or Crohn's disease (CD), aged 16 years and above. Demographic data, Partial Mayo Score (PMS) or Harvey Bradshaw Index (HBI), CRP, fecal calprotectin and type of anti-TNF-a agent were recorded. SDC were measured using automated in-house methods at Oslo University Hospital. Therapeutic serum concentrations were defined as 3–8 mg/L for IFX and 5–12 mg/L for ADA.
**Results:** In total, 210 patients were included, of which 73 (34.8%) had UC and 137 (65.2%) CD. Median (range) age was 37 (16–78) years and 57.6% were men. Median duration of treatment was 25 (2–98) months for UC, and 38 (2–164) for CD. Twenty-four (33%) patients with UC and 103 (72.5%) with CD received ADA, 49 (67%) UC- and 39 (27.5%) CD patients received IFX. In the ADA group, subtherapeutic SDC were present in 16.7% (UC) and 27.7% (CD). In the group receiving IFX, subtherapeutic SDC were present in 23% (UC) and 30.3% (CD). CD patients treated with ADA with SDC $<5$ mg/L had a significantly higher median fecal calprotectin- and CRP-levels compared to those with SDC $\geq 5$ mg/L ($p=0.005$ and $p=0.003$, respectively). CD patients treated with IFX with SDC $<3$ mg/L had higher CRP compared to patients with SDC $\geq 3$ mg/L ($p=0.003$). Fecal calprotectin levels were not significantly different. CRP and fecal calprotectin levels were not different in UC patients with subtherapeutic versus therapeutic SDC. We found no differences in disease activity indexes (HBI, PMS) between therapeutic and subtherapeutic SDC in either of the disease groups. In ADA treated patients, anti-drug antibodies were detected in 6.3% (CD) and 0% (UC) of the samples, whereas 3% (CD) and 14.6% (UC) of IFX treated patients presented with anti-drug antibodies.
**Conclusion:** In patients with CD subtherapeutic serum drug concentrations were associated with a significantly higher disease activity for both anti-TNF agents. These findings were not observed in the UC cohort.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1428 TUBERCULOSIS INFECTION IN AN INFLAMMATORY BOWEL DISEASE COHORT OF PATIENTS RECEIVING ANTI-TNF THERAPY IN A MODERATE TO HIGH TUBERCULOSIS INCIDENCE AREA IN EUROPE

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**Introduction:** Portugal has been considered a high incidence area for tuberculosis (TB) until 2000 and since then TB has been declining from 44.1 to 22.9 cases per 100 000 inhabitants, which is still higher than the average incidence in Europe. The incidence in urban centres, as is the case of our hospital, is also higher. Inflammatory bowel disease (IBD) patients receiving anti-tumor necrosis factor $\alpha$ (anti-TNF$\alpha$) are at increased risk for active TB.
**Aims & Methods:** We aimed to study the prevalence of latent (LTBI) and active TB in an IBD cohort under anti-TNF living in an intermediate to high TB incidence area. Retrospective cohort study of IBD patients receiving anti-TNF$\alpha$ from May 2001 to September 2015. Demographic, clinical, laboratorial and radiological data were collected from patients' medical records. LTBI was diagnosed when there was a positive tuberculin cutaneous test (TCT) or Booster (induration $\geq 5$ mm) or, since 2005, interferon gamma releasing assay (IGRA), and no radiological or clinical evidence of active TB.
**Results:** 101 patients were included with a mean age of 40.6±13.8 years, 58.4% were female. 78.2% had Crohn's disease, 19.8% had ulcerative colitis and 2.0% inflammatory bowel disease unclassified, with a median duration of disease of 10,5 years (IQR 6.3–15.9). 74.2% were on immunosuppressors when anti-TNF$\alpha$ was started. TCT was positive in 12.9% with TCT booster and IGRA diagnosing LTBI in further 1.0% of the patients each. Isoniazid was used in all 14.9% LTBI patients. Active TB was diagnosed in 3.0% ($n=3$), but the incidence of active TB in patients starting anti-TNF$\alpha$ after 2005 was only 1.2%. The mean age at diagnosis of TB was $44.0 \pm 7.9$ years. Two patients were anti-TNF$\alpha$ naives; two patients were under infliximab and one under adalimumab with a mean duration of anti-TNF therapy of $53.7 \pm 8.6$ months. TCT was negative in all 3 patients and IGRA was not available at the time of starting anti-TNF$\alpha$ in 2 (2001–2002). Two patients presented extrapulmonary TB (miliar and pleural). None of the patients died and one restarted anti-TNF one year after TB diagnosis.
**Conclusion:** Active tuberculosis in IBD patients receiving anti-TNF$\alpha$ in an intermediate-high incidence area was 3.0% and the infection was most frequently extra-pulmonary. Excluding and treating LTBI before anti-TNF$\alpha$ as recommended failed to eliminate the risk of active TB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1429 CUMULATIVE EXPOSURE TO ANTI-TNF ALPHA AND RISK OF CANCER

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**Introduction:** Although current evidence suggests no excess risk of cancer in patients with inflammatory bowel disease (IBD) treated with anti-tumour necrosis factor alpha (anti-TNF) agents, little is known about how the risk changes during time of exposure.
**Aims & Methods:** In this study we aimed to analyse the impact of the cumulative exposure to anti-TNF agents on cancer development in patients with IBD. Retrospective cohort study with 210 patients with IBD submitted to any duration of anti-TNF agents between 2003 and 2014. Demographic, clinical and medication data were collected. The primary outcome was the diagnosis of any cancer after initiation of an anti-TNF agent.
**Results:** Of the 210 patients 56.2% were women and the age at the end of follow-up was 43.24 + /- 13.98 years. Median follow-up time was 10.0 years, for 2442,3 persons-year. One hundred and ninety patients were diagnosed with Crohn's disease, 17 with Ulcerous Colitis and 3 with IBD unclassified. 94.8% were treated with azathioprine (average 1505.7 days) and 26.7% with methotrexate (average 1101.5 days) – total time of exposure to immunomodulators of 840,3 persons-year. One hundred and sixty three patients were treated with infliximab (average 1286.5 days) and 82 with adalimumab (average 1018.4 days): 788.7 years of exposure overall. Combination therapy with azathioprine was used in 132 (62.9%) patients (average 842.7 days) and with methotrexate in 44 (21.0%, average 686.5 days). Five patients had a personal history of cancer, and none of them recurred. Fourteen patients developed cancer during follow-up (6.7%; 5.7/1000 persons-year of follow-up and 17.8/1000 persons-year of anti-TNF therapy exposure): 1 colorectal, 2 fistula-related and 11 extra-intestinal cancers. Half of them were under azathioprine on diagnosis. Three (21.4%)

were diagnosed with less than 12 months of anti-TNF therapy and 8 (57.1%) with less than 24 months. The duration of exposure to anti-TNF, in days, was not associated with excess risk of cancer (OR 1.0; p = 0.196; 95% CI = 0.999–1.000), even after adjustment for age, smoking, time from diagnosis and exposure to azathioprine.
**Conclusion:** In patients with IBD, duration of exposure to anti-TNF therapy was not associated with excess risk of cancer. The potential increase in the risk of cancer with this therapy does not seem to be associated with its duration.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1430 ANEMIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: EFFECT OF ANTI-TNF THERAPY


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**Introduction:** Anemia represents the most common systemic complication of inflammatory bowel disease (IBD) and results from a combination of complex mechanisms, though iron deficiency and inflammation play major roles.
**Aims & Methods:** We aimed to analyze the prevalence and severity of anemia in a cohort of IBD patients and to determine the impact of anti-tumor necrosis factor (TNF) therapy on hemoglobin (Hb) levels. Retrospective study of an adult IBD cohort assigned to start anti-TNF therapy. Demographic, clinical and laboratorial (prior starting anti-TNF and after six months of therapy) data were collected from patients medical records. Anemia was defined as an Hb level lower than 12 g/dL in women and 13 g/dL in men; it was classified as mild (Hb $\geq$ 10 g/dL), moderate (Hb between 8–10 g/dL) or severe (Hb $\leq$ 8 g/dL).
**Results:** 85 patients were included, 57.6% female, with a mean age 35.5 ± 13.9 of years. 76.5% of patients had Crohn's disease (27.1% with fistulising phenotype) and 23.5% Ulcerative Colitis. At baseline, 87% of patients were under immunomodulators, 72.9% started Infliximab and 27.1% started Adalimumab. The prevalence of anemia was 58.8%. Anemia was considered mild in the majority of cases (42.4%) and severe in 11.8%. 8% of patients were under iron supplementation. At baseline, Hb levels correlated inversely with C-reactive protein levels (Spearman's rho -0.345, $p < 0.005$) and sedimentation rate (Spearman's rho -0.467, $p < 0.005$). We found a statistically significant difference in Hb levels before and after 6 months of being under anti-TNF therapy (11.7 g/dL Vs. 12.7, $p < 0.005$), with a significant decrease on the prevalence of anemia (58.8% Vs. 35.2%, $p < 0.005$). Fistulizing Crohn's disease (CD) was associated with anemia ($p = 0.04$). In contrast, gender, IBD type, CD location, UC extension or previous immunosuppression were not associated with anemia prevalence at baseline.
**Conclusion:** Anemia is a prevalent condition in the IBD population, irrespective of IBD type. A CD penetrating behavior is associated to the presence of anemia. High levels of inflammation are related to lower Hb levels. Anti-TNF therapy successfully improves Hb levels and is associated to a decrease in the prevalence of anemia.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1431 INFLIXIMAB BIOSIMILAR CT-P13 THERAPY IS EFFECTIVE IN MAINTAINING CLINICAL AND ENDOSCOPIC REMISSION IN CROHN'S DISEASE AND ULCERATIVE COLITIS – EXPERIENCES FROM A SINGLE CENTER


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**Introduction:** CT-P13, the first biosimilar monoclonal antibody to infliximab (IFX) has previously been confirmed to be efficacious in inducing remission in inflammatory bowel disease (IBD) patients.
**Aims & Methods:** The aim of this study was to assess the efficacy and safety of maintenance CT-P13 therapy in Crohn's disease (CD) and ulcerative colitis (UC). Patients diagnosed with CD and UC, who were administered CT-P13, were prospectively enrolled. Clinical outcome was estimated at fixed appointments throughout the 54-week treatment period. In UC, control sigmoideoscopy was performed at week 14 and week 54 to assess mucosal healing. In CD, control endoscopy was performed at week 54. Predictive factors, like CT-P13 trough levels at week 2, 6 and 14, antibody positivity at week 2, 6 and 14, C-reactive protein (CRP) level, concomitant steroid and azathioprine therapy, previous use of anti TNF, need of dose intensification and endoscopic remission for disease outcome at week 54 were statistically evaluated.
**Results:** Twenty-eight CD and 29 UC patients were included in the study of which 27 CD and 25 UC patients completed the induction therapy and 25 CD and 21 UC patients completed the 54-week treatment period. In CD, clinical response was achieved in 96.4% of the patients at week 14 and in 80% at week 54. Loss of response developed in 20% of the patients at week 54. In UC, clinical response was achieved in 82.8% of the patients at week 14 and in 62% at week 54. Rate of loss of response was 38% at week 54. Mucosal healing was shown in 74% of the patients at week 14 and in 68.8% at week 54. Overall, infusion reaction occurred in 14.3% of CD and 17.2% of UC patients. Bowel resection had to be performed in 2 CD patients and colectomy was needed in 3 UC patients throughout the treatment period. One UC patient died after the 2nd infusion because of azathioprine-induced myelosuppression. Dose intensification was the only factor associated with lower response rate in UC. None of the examined parameters were predictive to worse outcome in CD.
**Conclusion:** Our results confirm that CT-P13 is safe and effective in maintaining both clinical and endoscopic remission. Dose intensification was the single parameter that influenced disease outcome in UC.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1432 CLINICAL EXPERIENCE WITH VEDOLIZUMAB IN ANTI-TNF REFRACTORY IBD PATIENTS


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**Introduction:** Idiopathic inflammatory bowel disease (IBD), including Crohn's disease (CD), ulcerative colits (UC) and indeterminate colitis, are chronic inflammatory disorders defined by distinctive clinical, pathological, endoscopic and radiological features[1]. Treatment options for IBD include glucocorticoids for induction and treatment to induce recovery in relapse phase, immunosuppresive agents (i.e. azathioprine, mercaptopurine or methotrexate) and tumour necrosis factor antagonists (Anti-TNF). At times, we encounter patients in our clinical practice who had primary loss of response or secondary loss of response on treatment with Anti-TNF. Further investigations looking into this would include endoscopic and radiologial evaluation, as well as the use of therapeutic drug monitoring and check for antibody assay. The approval of Vedolizumab (VDZ) in 2014 for the treatment of moderate to severe Inflammatory Bowel Diease offers gastroenterologists a gut-specific biologic alternative to anti-TNF therapy in patients with refractory disease. Gut selective blockade of lymphocyte trafficking by VDZ, an $\alpha 4\beta 7$ integrin antibody, has been shown in clinical trials to offer effective induction and maintenance therapy in both ulcerative colitis and Crohn's disease [2,3] and a potential role as a rescue therapy post anti-TNF therapy [4,5].
**Aims & Methods:** We evaluated the efficacy of VDZ in a cohort of anti-TNF refractory IBD patients attending three teaching hospitals affiliated with Royal College of Surgeons in Ireland (RCSI). VDZ was administered intravenously at weeks 0,2,6 and 8 at a dose of 300 mg. Patients' characteristics and disease severity at first VDZ infusion and clinical response at week 12 post treatment were assessed. Clinical response among CD patients was assessed using the Harvey Bradshaw Index (HBI) and the Mayo score was used for UC patients. The data was obtained from the patients' charts and from patients when they attended the outpatient's review clinic pre and post commencement of VDZ infusions.
**Results:** Between November 2014 and March 2016, 19 patients (13 CD and 6 UC, 12 females and 7 males) received a total of 88 VDZ infusions. The mean age for our VDZ cohort was 36 years (range 20 – 55). There were two patients who were started on VDZ recently and have not reached week 12 of treatment yet. All 19 patients had undergone prior anti-TNF treatment, including 15 patients (79%) who had undergone both infusion and subcutaneous anti-TNF therapies. Thirteen patients were on concomitant immunomodulators (68%), while 8 patients (42%) had prior colonic resections. The mean pre-VDZ baseline HBI was 8 and Mayo score was 9. At week 12,10 of our 11 (91%) CD patients showed $\geq$ 3 point reduction in their HBI and 5 of our 6 (83%) UC patients had $\geq$3 point reduction in their Mayo scores. 15 out of 17 patients (88%) had shown clinical response. There were no reported infusion reactions or adverse events among our VDZ cohort.
**Conclusion:** Vedolizumab is safe, well tolerated and effective in our refractory IBD cohort all of whom had failed or lost response to prior anti-TNF therapy. Despite clinical trials suggesting superior efficacy among anti-TNF naive IBD patients, in clinical practice VDZ remains second-line therapy to anti-TNF.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1433 PERCEPTION FROM PATIENTS WITH ULCERATIVE COLITIS OR CROHN'S DISEASE TOWARDS THE PERFORMANCE OF BIOSIMILARS VERSUS BIO-ORIGINATORS

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**Introduction:** While the clinical impact of biosimilar substitution on patients with ulcerative colitis (UC) and Crohn's disease (CD) is being investigated by several clinical trials, evidence on how patients perceive biosimilars as treatment options and their satisfaction on the effectiveness is sparse.

**Aims & Methods:** We aimed to assess and compare the satisfaction of patients receiving a biosimilar and patients receiving a bio-originator. The Adelphi Biosimilars Therapy Insight Programme uses a well-established methodology, similar to that used in over 100 separate projects, and contains real-world, cross-sectional survey data from 25 German gastroenterologists who currently prescribe biosimilars, collected in Q4 2015 - Q1 2016. Gastroenterologists completed patient record forms (PRFs) about their UC and CD patients who were either receiving a bio-originator or a biosimilar of the same molecule. The PRF contained detailed questions on diagnosis, severity of condition and symptoms. Patients were then invited to complete a patient self-completion form containing questions on demographics and level of satisfaction with their current treatment.

**Results:** A total of 136 patients with UC or CD were included in this analysis, with 70 (51%) receiving a biosimilar and 66 (49%) receiving a bio-originator at time of survey. Demographically, patients on a biosimilar or a bio-originator did not differ significantly in terms of age, gender, ethnicity, and BMI. They also had similar symptom duration and current disease severity. Patients were asked to consider all aspects of the current treatment (effectiveness, safety, and quality) and almost all patients on bio-originators (91%, $n = 60$) felt satisfied they were receiving the best treatment compared to 79% of patients on a biosimilar ($p = 0.0486$). When asked about their perception of their current drug's performance on controlling their symptoms, 26% of those on a bio-originator responded that they were ''Very satisfied'', compared to 13% of patients on a biosimilar, but the difference is not significant ($p = 0.0580$). Nonetheless, this is consistent with the physicians' impression where satisfaction with bio-originators' control of patients' symptoms was higher (''Very satisfied'': 30% vs 16%, $p = 0.0446$).

**Conclusion:** A significantly larger proportion of patients who were receiving a bio-originator felt satisfied about the safety, clinical effectiveness and manufacturing quality of the drug than did the patients receiving a biosimilar. Biosimilars have only recently been approved for treating UC and CD. There isn't a lot of experience using them yet. Patients' preferences should be considered in treatment decisions. The benefit of cost-saving of biosimilars should not be achieved at the price of compromised patient satisfaction.

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E. Sullivan: Emma Sullivan received consultancy fees from Merck & Co., Inc. There is no other conflict of interests.
J. Piercy: James Piercy received consultancy fees from Merck & Co., Inc. There is no other conflict of interests.
J. Waller: John Waller received consultancy fees from Merck & Co., Inc. There is no other conflict of interests.
C. Black: Christophe Black is an employee and also owns stocks at Merck & Co., Inc. There is no other conflict of interests.
S. Kachroo: Sumesh Kachroo is an employee and also owns stocks at Merck & Co., Inc. There is no other conflict of interests.

## P1434 WEIGHT DISTRIBUTION IN EUROPEAN PATIENTS WITH CROHN'S DISEASE IN ADELPHI 2015 DSP

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**Introduction:** While it is generally acknowledged that active Crohn's disease results in weight loss, there is a paucity of information on the weight distribution of Crohn's patients at the time of initiation of therapy with biologics and the difference between Crohn's patients whose disease is under control versus those patients whose disease is not under control. This research aims to describe the weight distribution in European countries in patients recently started on biologic therapy, to describe patients weights in patients whose disease is under control versus not under control and comparing these results with results obtained for the general population according the Special Eurobarometer Health and Food (Wave 64.3), a large, representative, survey conducted across the EU for the European Commission.

**Aims & Methods:** The Adelphi DSP is a retrospective, cross-sectional analysis of survey data of patients with Crohn's disease, conducted between December 2014 and March 2015. Gastroenterologists from the US, Italy, France, Spain, Germany and the UK completed Patient Record Forms (PRFs) for the next 8 presenting Crohn's patients; questions included: specific demographics, physician subjective levels of severity (mild, moderate, severe), remission status and current treatment received. Respondents were incentivized for survey completion. Average weights were calculated for Italy, Spain, France, Germany and the UK (EU-5). Since weight distribution in Italy, Spain and France are more similar according to the Special Eurobarometer, results for these countries were also pooled in order to improve the reliability of the estimate for these countries. Patients not in control of their disease were defined as having a physician subjectively defined disease severity of moderate to severe and documented as not currently being in remission in the patient record form (PRF). Patients in control of disease were defined as mild disease and being in remission in the PRF.

**Results:** There are 2350 CD patients in total within the Adelphi Real World CD DSP in Europe, of which 996 patients were receiving a biologic at the time of data collection.

**Table 1:** Average weight in kg (SD; N)

| | EU – 5 | | France – Italy - Spain | |
|---|---|---|---|---|
| | Male | Female | Male | Female |
| Patients on a biologic < 3 months | 71.2(12.84;76) | 58.8(11.79;77) | 69.7(12;51) | 58.6(13.12;42) |
| | 65 (13.08; 153) | 64.7 (13.63; 93) | | |
| Patients on biologic not in control | 71.7 (15.09; 167) | 60.8 (15.54; 155) | 70.9 (13.55; 94) | 61.1 (18.26; 87) |
| | 66.4 (16.23; 322) | 66.2 (16.67; 181) | | |
| Patients regardless of treatment not in control | 72.8 (17.38; 325) | 61.5 (17.38; 317) | 73.3 (19.01; 185) | 60 (14.87; 173) |
| | 67.2 (17.82; 642) | 66.8 (18.36; 358) | | |
| Patients regardless of treatment in control | 77.1 (18.59; 589) | 64 (17.45; 547) | 75.8 (17.1; 355) | 62.9 (16.89; 328) |
| | 70.8 (19.18; 1136) | 69.6 (18.17; 683) | | |
| Eurobarometer * | 71.48 | 69.7 | | |

*unweighted average

**Conclusion:** These results provide an accurate estimate of the average weight observed of Crohn's patients in the EU in the real-world setting, substantiate the fact that uncontrolled patients' average weight is lower than those of the average population, and substantiate the weight differential between patients in remission and patients with active moderate-severe disease. This study contributes to the scant literature in this area, informing our understanding of the disease in real-world settings of clinical care.

**Disclosure of Interest:** D. Naessens: Employee of Janssen Pharmaceutica NV
B. Hoskin: Consultant to Janssen Pharmaceutica NV
J. Lucas: Consultant to Janssen Pharmaceutica NV

## P1435 MYCOPHENOLATE MOFETIL IS A VALID OPTION IN HARD-TO-TREAT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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**Introduction:** Few studies evaluated the role of mycophenolate mofetil (MMF) in inflammatory bowel disease (IBD). In addition, they were mostly performed on patients with failure to thiopurines only, and none specifically focused on subjects with previous multiple intolerances and/or nonresponses to immunosuppressants (IM) and biologics.

**Aims & Methods:** The aim of this study was to evaluate efficacy and tolerability profile of MMF in patients with IBD and limited medical treatment options. This study was conducted at the Division of Internal Medicine of ''Villa Sofia-Cervello Hospital'', Palermo, a tertiary referral centre for IBD. All consecutive patients who started an off-label treatment with MMF from January 2014 to March 2016 were entered in a prospectively maintained database. All adverse events and clinical outcomes were reported. We defined as ''complete response'' the steroid-free clinical remission, and as ''partial response'' a clinical improvement with concomitant reduction or discontinuation of steroids. All clinical variables were assessed at univariate analysis in order to identify predictive factors of treatment success.

**Results:** Baseline features of the study population ($n = 24$) are summarized in table 1. All patients had at least one previous nonresponse to IM or biologics. In particular, 15 (62.5%) were non responders to at least one IM, and 22 (91.7%) to at least one biologic agent; 12 (50.0%) were not responder to at least one IM plus at least one biologic. In addition, 20 (83.3%) had a previous intolerance to at least one IM, and 13 (54.2%) to at least one biologic. At the time of initiation of MMF, 22 patients had a moderate to severe active disease (91.7%), two had clinically inactive disease but were steroid-dependent, and 21 (87.5%) were concurrently taking oral corticosteroids with a median dose of 15 mg/day of prednisone (range 5–37.5 mg). The median duration of total follow-up was 32 weeks (range 12–124). Four weeks after initiation of MMF therapy, a complete response was achieved in 4 patients (16.7%), while a partial response in 13 (54.1%). At the end of follow- up 12 patients (50.0%) remained on MMF. Six achieved and maintained steroid-free remission throughout the study period (25.0% of total), and a further 6 patients (25.0%) achieved a partial response with complete discontinuation of steroids. Twelve patients (50.0%) were considered as treatment failure, and five of them underwent surgery. Drug side-effects were experienced by 7 out of 24 of patients (29.2%), leading to MMF discontinuation in five of them. No factor was identified as predictive for treatment success with MMF at univariate analysis. There was a trend towards a

higher efficacy in patients with ulcerative colitis compared with Crohn's disease (63.6% vs. 38.5%), but this was not significant (p = 0.20).

| Variable | N = 253 |
|---|---|
| **Age (years). mean ± S.D.** | 41.4 ± 12.5 |
| **Male gender, n (%)** | 10 (41.7%) |
| **Smokers, n (%)** Never Current Ex | 18 (75.0%) 2 (8.3%) 4 (16.7%) |
| **Type of Disease, n (%)** Crohn's Disease Ulcerative Colitis | 13 (54.2%) 11 (45.8%) |
| **Localization of the disease, n (%) Crohn's Disease** Ileal Ileocolic Colic Upper gastrointestinal tract Perianal Disease **Ulcerative Colitis** Proctitis Left-sided Extensive | 2 (15.4%) 9 (69.2%) 1 (7.7%) 1 (7.7%) 5 (41.7%) 0 (0.0%) 7 (63.6%) 4 (36.4%) |
| **Behavior (Crohn's Disease), n (%)** Inflammatory Stricturing Fistulizing | 3 (21.3%) 5 (38.3%) 5 (38.3%) |
| **Previous resections (Crohn's Disease), n (%)** | 10 (76.9%) |
| **Extraintestinal manifestations, n (%)** | 8 (33.3%) |
| **Concurrent IBD medications at baseline, n (%)** Prednisone 5-Aminosalycilates Biologics (combination therapy) | 21 (87.5%) 9 (37.5%) 4 (16.7%) |
| **Previous Intolerances/Nonresponses, n (%)** Nonresponse to at least one IM or one biologic Nonresponse to at least one IM Nonresponse to at least one biologic Nonresponse to at least one IM plus at least one biologic Intolerance to at least one IM Intolerance to at least one biologic | 24 (100%) 15 (62.5%) 22 (91.7%) 12 (50.0%) 20 (83.3%) 13 (54.2%) |

**Conclusion:** In our prospective mid-term experience, MMF was successful and well tolerated in half of the patients with IBD and multiple previous failures to other IM and/or biologics.
**Disclosure of Interest:** A. Orlando: Served as an advisory board member for AbbVie, MSD, Takeda Pharmaceuticals and received lecture grants for AbbVie, MSD, Sofar, Chiesi, and Takeda Pharmaceuticals
All other authors have declared no conflicts of interest.

## P1436 RISK FACTORS FOR COLECTOMY IN ULCERATIVE COLITIS PATIENTS WITH SEVERE FLARE-UP

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**Introduction:** Surgery continues to play an important role in acute severe ulcerative colitis (ASUC). Determining risk factors predisposing to colectomy could help the clinicians to indicate surgical intervention at the appropriate time in patients with ulcerative colitis (UC).
**Aims & Methods:** Aim: to investigate different factors which may predispose to colectomy in ASUC. Methods: In this retrospective study, we evaluated every hospital admissions due to acute exacerbation of UC and requiring intravenous corticosteroid treatment between 2000 and 2015. Two groups of patients were individualized: those who underwent colectomy (Gl) and those who avoided surgery (G2). Different parameters were compared and statistically analyzed between the two groups. $P < 0.05$ was considered statistically significant.
**Results:** Of the 105 UC patients hospitalized during the study period, 43 (41%) met the criteria of severe ulcerative colitis (44% male and 56% female; median age: 37 years). The median disease duration was 48 months. Twenty-four patients (55.4%) had pancolitis, 15 (34.8%) had left-sided colitis and 4 (9.3%) had proctitis. Overall 30.2% of the patients underwent colectomy. Patients of G1 were characterized by the following features when compared to those of G2: younger age at UC diagnosis (median age 30 years vs. 44 years, p = 0.02), more frequently pancolitis at diagnosis (44% vs. 26%, p = 0.026), with lower albumin level at admission (24.2 g/l vs. 35 g/l, p = 0.01). No difference was found between the two groups when analyzing disease duration, body mass index, extra-intestinal manifestations presence and inflammatory laboratory parameters.
**Conclusion:** Our results suggest that severe UC patients with younger age at diagnosis, pancolitis and hypoalbuminemia have a higher likelihood of requiring colectomy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1437 THE PROGNOSTIC FACTORS AND OUTCOMES OF RE-OPERATION WITHIN 6 MONTHS IN PATIENTS WITH INTESTINAL BEHCET'S DISEASE

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**Introduction:** Patients with intestinal Behcet's disease (BD) who received surgical treatment often require reoperation. However, there have been no studies on the prognostic factors and outcomes of reoperation timing in the patients with intestinal BD.
**Aims & Methods:** We evaluated 53 patients who received colorectal reoperation with intestinal BD between 2006 and 2016. We sought to compare between those requiring early surgical resection within 6 months and those over 6months after the initial bowel surgery and to determine the prognostic factor for early reoperation.
**Results:** Seventeen patients (32.1%) received reoperation within 6 months, and 36 patients (67.9%) received reoperation after 6 months. The early reoperation group with intestinal BD had significantly higher perioperative ESR and C-reactive protein (CRP) levels than the late reoperation group (P = 0.010; 74.7 ± 34.2 vs 46.9 ± 35.5, P = 0.001; 71.9 ± 17.4 vs 37.7 ± 6.4). Variables including male gender, emergency surgery at first operation status, and high ESR and CRP levels were significant prognostic factors in univariate analysis; however, after the multivariate analysis, high CRP level was the only independent factor for early reoperation (P = 0.024; adjusted HR, 1.017; 95% CI, 1.002–1.033). The mortality rate between the 2 groups was not significantly different using log-rank test. (P = 0.122)
**Conclusion:** Perioperative high CRP level was the prognostic factor of early reoperation (within 6 months) for patients with intestinal BD after bowel respective surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1438 OUTCOMES OF ABDOMINAL RESECTIVE SURGERY FOR CROHŃS DISEASE: IMPACT OF BEHAVIOUR AND TREATMENT

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Introduction: The majority of patients with Crohńs disease require intestinal resections during the course of their disease. It is still unclear whether disease behavior and/or the type of treatment impact on the reoperation rate.
Aims & Methods: Methods: We retrospectively reviewed the charts of all 341 Crohńs disease patients who had resective surgery at our center from 2000 to 2014. Kaplan-Meier analysis was performed over this 14 year period. For the statistics SPSS version 20.0 was used.
Results: Results: The male/female ratio was 165/176 (48.4/51.6%). The median age at diagnosis was 24 years and at index operation it was 37 years. One-hundred patients exhibited stenosing and 241 penetrating behavior. Perianal disease was reported in 93 cases (27.3%). Prior to surgery, treatment included biological agents (anti-TNF), azathioprine (AZA) and corticosteroids in 17.6%, 45.7% and 53%, respectively. Smoking habits were reported in 28.4%. The distribution of surgical procedures at the index operation was ileocecal resection (n = 154), resection of small bowel (n = 40) or colon (n = 122) and combined (n = 24). Overall, 97 patients required at least one more operation (uncensored) whereas 188 had no reoperation (censored) at the date of their last follow-up. In 56 cases (16.4%) no follow-up data were available. Of the 97 operations 71 were resective and 26 cases with non-resective surgery (mostly anal fistula) were excluded from the Kaplan-Meier analysis. Forty-six experienced one re-resection, 21 had two, 3 had three and 1 had 7 re-resections. Cumulative resective surgery-free survival tended to be superior in stenosing versus penetrating course of disease (p = 0.07). The Kaplan-Meier analysis showed comparable re-resection rates following small bowel and ileocecal resections but colonic resections had the highest re-resection rates (p = 0.0000053). Also, the preoperative use of steroids and AZA before index operation had no impact on re-resection rates (p-value = 0.97 and 0.74 respectively). In contrast, in the cohort that had required anti-TNF agents preoperatively, there was a trend to higher reoperation rates (p = 0.055), whereas the presence of granulomata and active smoking had no significant impact (p = 0.11 and 0.39 respectively). However, postoperative azathioprine and anti-TNF appeared to delay resective surgery (p = 0.13 and 0.12, resp.).
**Conclusion:** Penetrating disease, colonic resection and requirement of preoperative anti-TNF are indicators of poor prognosis with repetitive resection (s).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1439 PILOT STUDY ORAL ADMINISTRATION OF LACTOBACILLUS CASEI DG FOR 8 WEEKS AFTER ILEOSTOMY CLOSURE TEND TO DECREASE THE ACTIVATION LEVELS OF MACROPHAGES AND DENDRITIC CELLS IN ILEAL POUCH MUCOSA

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**Introduction:** An imbalance in gut microbiota seems to contribute to the development of ulcerative colitis (UC) and, after the restorative proctocolectomy to chronic pouchitis. Although it has been suggested that probiotic supplementation is an effective approach to colitis, its effects on activation of dendritic cells, macrophage and T cells in the ileal pouch mucosa have never been explored
**Aims & Methods:** To evaluate the effect of *Lactobacillus casei* (*L. casei*) DG, a probiotic strain, supplementation on activation state of dendritic cells, macrophage and T cells in the ileal pouch mucosa.
Twelve UC patients who had restorative proctolectomy accepted to be enrolled in this prospective pilot study. They received a daily oral supplementation of *L. casei* DG (24x109 CFU) for 8 weeks from the ileostomy closure to a pouch endoscopy after 8 weeks. Biopsies were collected from the pouch mucosa to assess activation of dendritic cells, macrophage (CD40 and CD80 expression) and T cells (CD69 expression) by dual staining flow cytofluorimentry. Wilkoxon match paired rank test was used to compare the results at the two time points
**Results:** No patients showed any sign of clinically active pouchits the two time points. Following 8 weeks of oral *L. casei* DG administration the expression of the costimulatory molecules CD40 and CD80 on the surface of CD163 + cells (macrophages) tended to be lower (62 [IQR: 56–149] vs 51 [IQR: 29–85], $p = 0.07$ and 69 [IQR: 52–135] vs 45 [IQR: 25–93], $p = 0.07$, respectively). Similarly CD40 tended to be less expressed on the surface of CD1a + cells (dendritic cells) (91 [IQR: 44–195] vs 37 [IQR: 31–90], $p = 0.07$). No significant variation was observed in CD4 + and CD8 + T cells activation
**Conclusion:** Supplementation of *L. casei* DG seems to decrease the activation of and mucosal-associate innate immune cells in ileal pouch mucosa. The results of this pilot study encourage the design of a randomized controlled trial aimed to decrease the risk of chronic pouchitis
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
## OTHER LOWER GI DISORDERS III – POSTER EXHIBITION

### P1440 WHOLE METAGENOMICS SEQUENCING GIVE NEW INSIGHTS ON RELATIONSHIPS BETWEEN FODMAPS INTAKE, GUT MICROBIOTA AND SEVERITY OF SYMPTOMS IN IRRITABLE BOWEL SYNDROME

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**Introduction:** Many studies have investigated the gut microbiota composition in irritable bowel syndrome (IBS), mostly using 16 S sequencing. However, knowledge about gut microbiota metabolic capacities and the association with diet in IBS is limited. We previously reported an association between IBS symptom severity and gut microbiota composition (Tap UEGW 2015). We aimed to assess the genetic content of this microbiota signature for IBS severity using a whole metagenomics sequencing approach
**Aims & Methods:** 144 subjects (106 IBS patients and 38 healthy subjects) were included in this study. Exhaled $H_2$ and $CH_4$, oro-anal transit time, psychological and gastrointestinal symptom severity were determined. FODMAPs intake was calculated based on 4-days food diaries from a subset of 75 subjects (65 IBS and 10 healthy). Metagenomic analysis of fecal microbiota was generated using the SOLiD technology. Metagenomic reads were mapped to the MetaHIT database in order to quantify metagenomic species (MGS) and their associated genes. MGS gene content was also used to assess a specific genomic lineage for each subject. In addition to classical numerical ecology and multivariate statistics, co-inertia analysis between MGS lineages and individual FODMAPs (fructose, fructans, Galacto-Oligo-Saccharides (GOS), Lactose) was performed.
**Results:** A total of 55 MGS were identified to be associated with the microbiota signature for IBS symptom severity. Based on their genetic content, 20 MGS could be further divided into 40 genomic lineages. Within some MGS, we found that two different genomic lineages (equivalent to subspecies) could be oppositely associated with symptoms severity. Although FODMAPs intake was not directly associated with health status in our study, co-inertia analysis showed that MGS associated with IBS severity could be linked with intake of GOS and fructans, but not lactose. The strongest association was found between one specific genomic lineage of Roseburia intestinalis associated with IBS severity and GOS intake.
**Conclusion:** Whole metagenomics sequencing allowed us to better characterize the gut microbiota signature associated to IBS symptom severity. Specific genomic lineages derived from MGS and their association with intake of FODMAPs deserve further functional exploration. This study supports the relevance of analyzing microbiota at lower taxonomic level than species and opens opportunities for personalized nutritional recommendations.
**Disclosure of Interest:** J. Tap: Julien Tap is employee of Danone Research
M. Derrien: is employee of Danone Research
B. Le Nevé: is employee of Danone Research
J. Doré: has received a financial support for research by Danone Research, Pfizer and PiLeJe, and served as a consultant/Advisory Board member for Danone Research and AlphaWasserman, Enterome Bioscience and MaaT Pharma
L. Öhman: L. Öhman has received a financial support for research by Danone Research and served as a consultant for Genetic Analyses (Lecture fee (s): Abbvie, Takeda)
H. Törnblom: Consultant/Advisory Board member for Almirall, Danone and Shire.
M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/ Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall.
All other authors have declared no conflicts of interest.

### P1441 ESCHERICHIA COLI NISSLE 1917 REINFORCES INTESTINAL EPITHELIAL BARRIER AND PREVENTS PERMEABILITY ALTERATIONS INDUCED BY CYTOKINES AND PAR-2 ACTIVATION: AN IN VITRO STUDY

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**Introduction:** The integrity of intestinal epithelial barrier is key to avoid the entrance of pathogens and antigens in the deeper mucosal layers. The "leaky gut" plays a crucial role in the pathogenesis of inflammatory bowel diseases (IBD) and potentially also in the pathophysiology of irritable bowel syndrome (IBS). Probiotics are live microorganisms widely used in clinical practice, although their mechanism of action remains unclear. Escherichia coli Nissle 1917 (EcN) is a probiotic with demonstrated efficacy in the maintenance of remission of ulcerative colitis, although its mechanism of action is incompletely known.
**Aims & Methods:** The aim of the present study was to characterize the mechanism of action of EcN in the prevention of increased intestinal permeability caused by known inflammatory stimuli. We used an in vitro model of intestinal permeability using CaCo-2 cells. Two concentrations of EcN ($10^8$ and $10^6$) were applied to CaCo-2 to evaluate their effect on paracellular permeability. The ability of EcN in the prevention of increased epithelial monolayer permeability induced by SLIGRL (a protease-activated receptor-2 activating peptide), tumor necrosis factor (TNF)-a and interferon (IFN)-g was investigated. Paracellular permeability was evaluated using sulfonic-acid-conjugated to fluorescein (FITC). mRNA expression of tight junction proteins, zonula occludens-1 (ZO-1), occludin, claudin-1, claudin-2 and junctional adhesion molecule-A (JAM-A) was assessed by qPCR
**Results:** EcN induced a dose-dependent reinforcement of CaCo-2 monolayer of 52% ($10^8$) and 32% ($10^6$) compared to untreated CaCo-2 (CTR). SLIGRL 200 uM induced a 7-fold increase in CaCo-2 permeability compared to CTR; the co-incubation of SLIGRL and EcN induce a recovery of epithelial integrity of 77% for $10^8$and 63% for $10^6$ compared to SLIGRL alone. SLIGRL 50 uM increased epithelial permeability (83%) compared to CTR and this effect was reverted by the co-incubation with EcN. TNF-a and IFN-g induced an increase in CaCo-2 permeability compared to CTR (4- and 1-fold respectively) reverted by EcN but not in a dose-dependent way qPCR analysis showed EcN induced a significant increase in occludin, JAM-A and claudin-1 compared to CTR ($P < 0.05$), while a borderline effect was observed on ZO-1 expression. No effect was observed on claudin-2 expression. The co-incubation of EcN with TNF-a induced a significant recovery in ZO-1 and occludin expression compared to TNF-a alone ($P < 0.05$). Co-incubation of EcN and SLIGRL induced a borderline increase of JAM-A and decrease of MLCK expression compared to SLIGRL alone.
**Conclusion:** EcN reinforces epithelial integrity acting on different tight junction proteins. In the presence of inflammatory stimuli, which increase epithelial monolayer permeability, EcN exerts a marked protective role. Future studies should extend these observations to exploit EcN therapeutic potentials in IBS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1442 A PERIANAL SWAB-BASED PCR ASSAY FOR DIAGNOSING COLONIZATION BY PATHOGENIC C.DIFFICILE

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**Introduction:** C.difficile is a Gram-positive anaerobe that can cause life-threatening diarrhoea. There is no current method with which to identify pathogenic C.difficile colonisation (PCDC) quickly. In order to be pathogenic, C.difficile must have the ability to make toxin B.

**Aims & Methods:** We have designed and validated an rtPCR assay targeting the toxin B with which to diagnose PCDC quickly using a perianal swab. Perianal swabs were taken prospectively from 99 patients with proven stool culture-positive C.difficile infection (CDI) within 24 hours of diagnosis. DNA from swab tips was extracted using the automated QIAsymphony platform. Half of the DNA extracts from patients with CDI along with control C.difficile DNA were used to optimise an rtPCR assay using primers targeting the C.difficile toxin B gene. PCRs were run as 10$\mu$L reactions on 96 well plates in duplicate and the volume of extract per reaction was varied (1–3$\mu$L). PCR positive was defined as: amplification curve crossing the threshold at $<40$ cycles, $<0.5$ CT difference between duplicates, melting points to be $\pm$ 1.25OC of that of C.difficile DNA and no amplification in negative controls. PCR positivity was compared to culture result as the gold standard. Once optimised, the assay was validated using the remaining 48 DNA extracts from CDI patients and extracts from swabs taken from 11 control patients with C.difficile-negative diarrhoea.

**Results:** In optimisation, assay sensitivity increased as more DNA extract was added (40%, 62% and 78% for 1$\mu$L, 2$\mu$L and 3$\mu$L respectively, $p = 0.0042$). The 3$\mu$L assay showed 92% efficiency and linearity of 0.997 was selected for the validation study. For validation using perianal swabs from 48 patients with proven CDI and 11 C.difficile stool culture- negative patients, assay sensitivity was 69%, specificity 93%, positive predictive value (PPV) 97% and negative predictive value (NPV) 48%.

**Conclusion:** We designed an rtPCR assay to identify C.difficile toxin B in DNA extracted from perianal swabs taken from patients with diarrhoea. Although the sensitivity in the validation experiments was low (69%), the high specificity and PPV mean that the assay may have clinical applicability. As almost all patients testing positive with the PCR swab test will be colonised with pathogenic C.difficile, they could be isolated on hospital admission to reduce the chance of nosocomial spread. Patients testing positive could also be prospectively followed to see if colonization with pathogenic C.difficile on admission is a risk factor for subsequent C.difficile-induced diarrhoea (CDI), poorer outcome if diagnosed with CDI, or relapsing disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1443 METAGENOMIC CHARACTERISATION OF GUT MICROBIOTA IN IBS PATIENTS

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**Introduction:** Irritable Bowel Syndrome (IBS) is a gastrointestinal (GI) disorder that exhibits different GI and neurological symptoms such as abdominal pain, diarrhoea, constipation and mood disorders. The gut microbiota play an important role in modulating the communication between the Central Nervous System (CNS) and the GI tract, the so-called microbiota-gut-brain axis. In this context, IBS is a clear example of the alteration of the fine equilibrium between the gut microbiota and the CNS. Furthermore it has been observed that probiotic treatments of IBS results in the relief of GI and neurological symptoms, thus we could hypothesize the direct impact of the gut microbiota on IBS physiopathology. Since the IBS bacterial gut microbiota has been extensively studied we focused our attention also on the fungal counterpart of the gut microbiota, "the mycobiota".

**Aims & Methods:** The aim of the present work was to evaluate biodiversity in bacterial and fungal microbiota of a cohort of 20 IBS subject and 21 healthy subject (HS) through culture-based and metagenomics approaches. The bacterial diversity that relies on DNA polymorphism has been performed by means of cluster analysis of ARDRA profiles. Moreover the absolute abundances of bifidobacteria and enterobacteria has been evaluated by qPCR. For IBS gut mycobiota characterization, fungal strains from IBS stool samples were isolated and identified by mean of ITS1–4 sequencing. Furthermore, isolates were phenotypically characterized to evaluate their resistance to GI tract stresses (temperature, low pH and oxbile resistance), while Candida isolates were further clustered by means of their RAPD profiles.

**Results:** The cluster analysis of ARDRA profiles showed that IBS bacterial microbiota clusters apart from HS microbiota. In addition we observed a 2.8-fold increase in the absolute abundance of enterobacteria in IBS subjects vs HS. The analysis of the gut mycobiota revealed significant differences in fungal isolates abundance in IBS subjects vs HS even if we did not find any significant difference in species richness. In particular, results showed an abundance of fungi (61.8% C. albicans), with a higher number of colony count 4.7 $\log_{10}$ CFU/g faeces in IBS subjects respect to HS faecal samples with 1.9 $\log_{10}$ CFU/g (48.75% C. albicans).

RAPD prolfile analysis of C. albicans and C. parapsilosis showed that IBS isolates clustered apart from HS isolates, suggesting their different genotypical background. Finally, we observed that IBS fungal isolates showed different phenotypical features with an increased ability to growth to high temperatures and low pH respect to isolates from HS.

**Conclusion:** Our results showed the presence of alterations in the microbial community structure of IBS subjects, both at bacterial and fungal level, respect to HS. The absolute abundance of enterobacteria in IBS subjects suggests their connection with putative inflammatory phenomena as previously observed in IBS and other pathologies (Lee and Park, 2014). The phenotypical characterization of IBS fungal isolates revealed that such isolates showed a different response in respect to GI-like stresses. Moreover we observed that C. albicans and C. parapsilosis isolates from IBS are both phenotypically and genotypically different from HS Candida isolates suggesting their putative different ecological distribution. Finally we could hypotesize that dysbiosis of the gut microbiota in IBS could be one of the driving factor in IBS pathophysiology that could be responsible of intestinal fungal population overgrowth.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### Reference

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## P1444 INCREASED ABUNDANCE OF BENEFICIAL BACTERIA IS ASSOCIATED WITH CLINICAL IMPROVEMENT IN PATIENTS RECEIVING RIFAXIMIN TREATMENT

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**Introduction:** Rifaximin is a non-absorbable antibiotic active against Gram + and Gram - bacteria which is also able to produce a favorable modulation of the gut microbiota[1,2,3,4,5]. However, it is still not clear if this beneficial effect could be associated with clinical improvement.

**Aims & Methods:** The aim of this study was to explore the correlation between gut microbiota modulation and symptoms improvement in patients undergoing rifaximin treatment. Rifaximin 1200 mg/daily was administered for 10 days to patients with ulcerative colitis (UC), Crohn's disease (CD), irritable bowel syndrome (IBS), diverticular disease (DD) and cirrhotics with hepatic encephalopathy (HE). Inclusion criteria: no exposure to antibiotics, pre-/pro-biotics and bowel colonoscopy preparation for at least one month, and omnivore normocaloric diet for at least one year. Fecal samples were collected and symptoms were assessed at baseline and at the end of treatment. Clinical improvement was evaluated by Mayo score for UC, CDAI for CD, IBS-SSS for IBS, GSS for DD, and West Haven classification for HE. Fecal microbiota composition was assessed by a metagenomic gene-targeted approach (16 S rRNA) using the Roche 454 GS Junior ad Qiime pipeline. Biostatistical analysis was performed using R-statistics packages.

**Results:** Twenty-five patients were included in the study. Clinical improvement was observed in 10 (40%) patients after rifaximin treatment. Nonmetric multidimensional scaling (NMDS) ordination on Bray Curtis distance highlighted a significant clustering of patients who experienced clinical improvement compared to those who did not ($p = 0.047$; PERMANOVA). Differential abundance analysis revealed an increased abundance of Faecalibacterium prausnitzii in case of symptoms amelioration after rifaximin treatment (improved post vs pre: $\log FC = 1.96$; $p = 0.05$; not improved post vs pre: $\log FC = -0.37$; $p = 0.810$). The post-treatment between-groups comparison confirmed a significantly higher abundance of Faecalibacterium prausnitzii in those patients whose symptoms improved after rifaximin ($\log FC = 4$; $p < 0.0001$). Clinical improvement was also paralleled by a significant increase in bacterial alpha-diversity ($p = 0.024$).

**Conclusion:** In patients with gastrointestinal and liver diseases clinical improvement consequent to rifaximin treatment is associated with the increase in Faecalibacterium prausnitzii abundance. The increase in beneficial bacteria may mediate rifaximin effects in different pathologic settings.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1445 DIRECT ISOLATION OF ORAL- AND TUMOUR-DERIVED FUSOBACTERIUM SPECIES IN PATIENTS WITH COLORECTAL NEOPLASIA

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**Introduction:** Fusobacterium nucleatum is a gram-negative, obligate anaerobe that is a typical resident of the oral microbiome. More recently, F. nucleatum has been associated with malignant and pre-malignant colorectal neoplasia in several metagenomic studies and plausible mechanisms of tumourigenesis have been proposed[1,2]. However, actual isolation of Fusobacterium from colorectal neoplasia has been extremely limited and no attempt has been made to isolate Fusobacterium from the oral and colorectal microbiomes in the same individual.

**Aims & Methods:** We prospectively recruited adult patients undergoing elective resection of colorectal neoplasia. An oral periodontal swab was taken pre-procedure and tissue biopsies were obtained from adenomas / carcinomas and adjacent macroscopically normal tissue following resection. Tumours were swabbed if insufficient tissue was available for biopsy. Oral swabs and tissue biopsies (or swabs) were inoculated onto Fusobacterium-selective culture plates and incubated in a strictly anaerobic environment before distinct colonies were isolated. Fusobacteria were initially identified by Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) mass spectrometry which was subsequently confirmed by 16s rRNA sequence analysis. Furthermore, DNA was extracted from available tissue samples and 16 s rRNA genes were sequenced using the Ilumina MiSeq platform.

**Results:** Between January 2014 and April 2015 samples were obtained from 36 patients undergoing resection of colorectal neoplasia (33 carcinomas, 3 adenomas). Tumour locations were 19 rectum, 11 ascending/caecum and 6 sigmoid colon. Oral swabs were obtained in 25 patients (72%), of which 15 (60%) yielded Fusobacterium isolates. Fusobacterium isolates (8 nucleatum, 2 gonidoformans) were also cultured from neoplastic tissue/swabs in 6 patients (17%) and normal mucosa in 4 patients (11%). In 2 (8%) patients, paired Fusobacterium isolates were obtained from both mouth and tumour. Metagenomic analysis revealed that Fusobacterium species were found in 8/23 tumour biopsies compared to 2/25 normal mucosal samples (35% vs. 8%, $p = 0.09$). However, of the 10 DNA positive biopsy samples, only 2 yielded Fusobacterium isolates on culture.

**Conclusion:** This is the first investigation to culture a significant number of Fusobacterium isolates from both the oral and tumour microbiomes of patients with colorectal cancer. Although metagenomic analysis demonstrated a trend towards overexpression of Fusobacterium on tumour tissue compared to healthy mucosa, the low rates of isolation from DNA positive tissue highlights the difficulty in culturing these fastidious organisms from clinical samples. Isolation from the oral microbiome was more successful and it will be interesting to make genetic comparisons between isolates from the oral and colorectal microbiomes where pairs were available.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1446 COMBINING FECAL IMMUNOCHEMICAL TESTING WITH THE GUT MICROBIOME IN COLORECTAL CANCER SCREENING

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**Introduction:** Many countries use fecal immunochemical testing (FIT) to screen for colorectal cancer (CRC). However, FIT has a low sensitivity for precancerous adenomas and serrated lesions. There is increasing evidence that fecal microbiota play a crucial role in CRC carcinogenesis. Therefore, we assessed if the fecal microbiome can be used as additional biomarker in FIT for CRC screening.

**Aims & Methods:** Positive FIT samples ($n = 200$) of a CRC screening cohort, involving average risk subjects aged 50–74 years, were analyzed for universal 16 S, and bacteria previously associated with CRC, Escherichia coli, Fusobacterium nucleatum, Bacteroides and Faecalibacterium prausnitzii, by qPCR. Stability of microbial content over time was analyzed, both in stool samples of a healthy volunteer, as well as in FIT-positive samples. The qPCR results were compared to findings at colonoscopy. Advanced neoplasia was defined as an adenoma with a diameter $\geq$10 mm, and/or with a $\geq$25% villous component, high-grade dysplasia and/or CRC.

**Results:** Of the FIT-positive samples, 20 had to be discarded for various reasons resulting in 180 samples. Colonoscopy outcomes are described in table 1. Fecal microbiome was stably measured with no significant decrease in fecal microbiota up to 6 days for *E. coli* ($p = 0.53$), F. nucleatum ($p = 0.30$), Bacteroides ($p = 0.05$) and F. prausnitzii ($p = 0.62$). No significant differences in fecal microbiome in FIT were found between screenees with and without advanced neoplasia ($p = 0.23$). Total bacterial load (i.e. 16 S) was significant higher in patients with CRC and high-grade dysplasia ($p = 0.006$). For other bacteria, relative to 16 S, no association was found with colonic lesions. Table 1. Most advanced lesion at colonoscopy of FIT positive screenees.

| Finding at colonoscopy | n (%) |
|---|---|
| Normal | 41 (22.4) |
| Serrated polyps | 25 (13.7) |
| Tubular adenoma < 10 mm | 59 (32.2) |
| Tubular adenoma >=10 mm | 33 (18.0) |
| (tubulo) villous adenoma | 14 (7.7) |
| High-grade dysplasia | 3 (1.6) |
| Colorectal carcinoma | 5 (3.3) |
| **Total** | **180 (100*)** |

*numbers do not add up exactly to 100% due to rounding

**Conclusion:** To the best of our knowledge we are the first to describe the use of measuring the gut microbiome in FIT for CRC screening. Our results show that the fecal microbiome can be measured in FIT-samples and remains stable for 6 days. Total bacterial load was higher in CRC and high-grade dysplasia. Our results show that different microbial content may be associated with different stages of disease. These results pave the way for further research to determine the role of microbiota in FIT, to increase FIT sensitivity.

**Disclosure of Interest:** S. Konstantinov: I do not know the specific conflict of interests of this author
All other authors have declared no conflicts of interest.

## P1447 THE INCIDENCE AND TREND OF CLOSTRIDIUM DIFFICILE INFECTION AT A JAPANESE UNIVERSITY HOSPITAL FROM 2005 TO 2014

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**Introduction:** Although the incidence of Clostridium difficile infection (CDI) is increasing worldwide, the incidence and trend of CDI in Japan remains uncertain. This retrospective cohort study evaluates the incidence and trend of CDI from 2005 to 2014 at a 678-bed university hospital in Japan.

**Aims & Methods:** Data on Clostridium difficile toxin assay results and the number of admission and discharge were collected from hospital databases. Annual hospital-onset, hospital-associated (HO-HA) CDI incidence and seasonal variation were evaluated. HO-HA CDI cases were defined as patients with symptom onset more than 48 hours after admission to the hospital.

**Results:** 126,396 patients were admitted with 2,130,436 patient-days at our hospital during the 10-year study period. Overall, there were 307 HO-HA CDI cases, a rate of 1.44 cases per 10,000 patient-days. Table shows annual incidence of HO-HA CDI. The incidence rate of HO-HA CDI was 1.29 in spring, 1.42 in summer, 1.56 in fall, and 1.48 in winter per 10,000 patient-days.

**Table:** CDI cases per 10,000 patient-days from 2005 to 2014.

| 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 |
|---|---|---|---|---|---|---|---|---|---|
| 1.83 | 1.46 | 1.98 | 1.41 | 1.01 | 1.19 | 1.18 | 1.44 | 2.13 | 0.72 |

**Conclusion:** The incidence of CDI was lower than that reported from hospitals in most Western countries. CDI incidence was not increased from 2005 to 2014, and did not significantly differ between seasons at a Japanese university hospital.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1448 METAGENOMICS ANALYSIS THE FUNCTION AND MOLECULAR MECHANISMS OF THE VARIABLE BACTERIA IN IBS-D AND DEPRESSION

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**Introduction:** Alteration of gut microbiota is related to Irritable Bowel Syndrome (IBS) and depression. Actually, depression often comorbid with IBS. In our previous study, we found that diarrhea-predominate IBS (IBS-D) and depression had the similar gut microbiota structure. However, whether the function of gut microbiota of IBS-D and depression is similar remains unclear.
**Aims & Methods:** To explore the difference of functional variation of gut microbiota between IBS-D and depression using metagenomics.IBS-D patients, depression patients and health controls were enrolled. Subjects with organic intestinal diseases, diabetes, obesity, cancer, history of abdominal operation and other psychological disorders and those who had taken probiotics, antibiotics or antidepressants in the 4 weeks before enrollment were excluded. Metagenome DNA were extracted from fecal samples and sequenced through Illumina HiSeq 2000. Genes were predicted using MetaGUN and further annotated using BLAST against the eggNOG database and the KEGG Orthology database. To calculate coefficient of correlation in the co-occurence network, SparCC was applied.
**Results:** Fecal samples were collected form 31 subjects (11 IBS-D, 10 depression and 10 health controls). The differential abundance of 54 gut microbiome genes in IBS-D group and 111 in depression group were identified. These genes are primarily associated with the metabolism of carbohydrate, amino acid, cofactors and vitamins, nucleotide, energy and membrane transport. The genes associated with pentose phosphate pathway (eda, hxlA), porphyrin and chlorophyll metabolism (cobU, cobP, cysG, chlD, chlI), mineral absorption (ATOX1) and base excision repair (tag) decreased in IBS-D only, whereas genes associated with metabolism of ascorbate and aldarate metabolism (garL, ulaA, ulaC, ulaB), galactose metabolism (gatA, gatB, gatC), bacteria secretion system (gspC, vasD, hcp, impK), folate biosynthesis (pabA, moaC, MOCS1), nitrogen metabolism (nrfC, narI, narJ, nifH), two component system (fliC, phoR, motA, narL, tsr, crp, desK, hydH) increased in depression only. In the network, the most intensive interaction was between the protein associated with carbohydrate transport and metabolism in health controls, while it was between the proteins associated with inorganic ion transport and metabolism, cell wall/membrane/envelope biogenesis and signal transduction mechanisms in IBS-D and depression, which can enhance bacteria virulence when overexpressed. The interaction between the proteins associated with defense mechanisms increased in depression but decreased in IBS-D.
**Conclusion:** The function of gut microbiota of IBS-D and depression differs from that of health controls, but the variation is different between IBS-D and depression in genes associated with metabolism functions, bacteria secretion and signal transduction together with co-occurrence network. It might be related to the different clinical features of IBS-D and depression.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1449 UNDISSOCIATED GELATINE TANNATE AND XYLOGLUCAN PREVENT GUT LEAKINESS AND MUCOSAL INFLAMMATION INDUCED BY LPS: INSIGHTS IN THE MECHANISM OF ACTION

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**Introduction:** Gelatine tannate (GT) and xylogucan (XG) are commercially available in several countries for the oral treatment of diarrhea in children and adults. However, the mechanism of action remains poorly understood.
**Aims & Methods:** Therefore, we aimed to investigate the effects of GT and XG treatment and the mechanisms of action involved in LPS treated rats, an animal model characterized by two common gastroenteritis features, namely the intestinal epithelial barrier impairment and mucosal inflammation. The parameters evaluated were 1) the severity of intestinal mucosal inflammation, 2) gut paracellular permeability, 3) tight junction proteins expression and 4) spatial localization of the commensal bacteria load in ileal and colonic sections. Male Wistar rats were orally treated with GT (250 mg/kg) or XG (12.5 mg/kg) or vehicle (water plus $Na_2CO_3$, p.o) 2 h before IP injection of LPS from *E. coli* (1 mg/kg). Jejunal tissue strips were collected to evaluate 1) mucosal inflammation by MPO activity measurement 2) paracellular intestinal permeability to FITC-dextran 4 KDa in Ussing chambers and 3) occudin and Jam-A protein expression levels by western blotting. The commensal bacterial load was determined by FISH technique in ileal and colonic samples.
**Results:** Compared with control, LPS administration promotes a significant increase ($p < 0.05$) of intestinal paracellular permeability associated with a decreased expression of occludin and JAM-A and a subsequent jejunal mucosal inflammation. LPS also induced mucus barrier impairment reflected by the close apposition of commensal bacteria to ileal and colonic epithelium. Both GT and XG significantly ($p < 0.05$) reduce the severity of LPS induced mucosal inflammation and jejunal hyperpermeability. However, both treatments did not prevent the LPS-induced occludin and JAM-A down regulation. Further, GT and XG treatments result to a containment of the commensal bacterial load at the external face of the mucus layer limiting the bacterial mucus layer invasion and contact between bacteria and intestinal epithelium.
**Conclusion:** In this study we show that GT and XG treatments prevent LPS-induced gut leakiness and subsequent intestinal inflammation. These beneficial effects result from a mechanical protection of the gut epithelium through a "coat"-forming ability which avoids the upload of adverse luminal factors through the intestinal epithelium and subsequent adverse consequences.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1450 PREDICTING TREATMENT FAILURE IN C.DIFFICILE INFECTION: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

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**Introduction:** C.difficile-induced diarrhea is often refractory to treatment and can be life-threatening. As yet, there is no prospectively derived tool with which to predict treatment failure (TF) in C.difficile infection (CDI).
**Aims & Methods:** We performed a fully powered, pragmatic, prospective observational study to create such a tool. Patients with confirmed CDI were consented to enter the study within 24 hours of testing positive.
Demographic data (including age, antibiotic and PPI use, smoking, ward type), clinical variables (pulse, PB, temperature) and blood test results (FBC, urea, creatinine, CRP, albumin) and faecal calprotectin on the day of diagnosis were collected. TF was defined as occurrence of any of: death while admitted, colectomy, ongoing diarrhoea at day 7, recurrent diarrhoea at < 30 days after initial CDI diagnosis. Case level re-structuring was used to account for missing data and forward stepwise binary regression to derive a predictive model. The model was internally validated by bootstrapping and assessed by Receiver Operated Characteristic (ROC) analysis.
**Results:** 122 patients were recruited and primarily treated by their routine clinical team with metronidazole (n = 89) or vancomycin (n = 29). 63 patients (52%) failed treatment: 28 died during their admission, 43 had continuing diarrhea at day 7, 16 had recurrent diarrhea within 30 days and 1 had a colectomy (some patients had TF on > 1 criteria). TF rate was the same whether metronidazole or vancomycin was primary therapy. Of the variables measured, only age and serum albumin predicted TF (age, $p = 0.029$; albumin, $p = 0.0001$). An equation with which to predict individual patients' risk of TF was then derived: for ease of clinical application, a simple read off table was derived allowing prediction of outcome using the patient's age and serum albumin. The model correctly predicted TF in 79% of cases. By ROC analysis, the model initially had an Area Under the Curve (AUC) of 0.76; in the internal validation assessment the AUC was 0.75.
**Conclusion:** A prospectively and internally validated tool with which to predict treatment failure in CDI has been derived. The tool consists of 2 variables (age and serum albumin) on the day of diagnosis of CDI. The predictive tool could be used to highlight those who might benefit from more intensive treatment, for example using fidaxomicin or faecal microbial transplant as primary CDI therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1451 A STABLE AND CLINICAL REPRESENTATIVE MOUSE MODEL OF CLOSTRIDIUM DIFFICILE–ASSOCIATED DISEASE

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**Introduction:** *Clostridium difficile* (*C.difficile*), a toxin-producing bacillus responsible for life-threatening diarrhea that leads to significant morbidity and mortality worldwide, has caused considerable social and economic burden.[1,2]*C.difficile*–associated disease (CDAD) has been studied in a number of animal species, including hamsters, guinea pigs, rabbits, germ-free mice and rats. Hamsters historically have been most widely used to investigate disease pathogenesis and treatment, but are not ideal models because they develop fulminant disease which can't well mimic clinical course of disease in human beings.[3,4]In recent years, the most frequently used model is conventional C57BL/6 mice, in which CDAD can be initiated by a mixture of antibiotics, and colonization may follow clindamycin and *C.difficile* challenge. But our previous study found that the range of severity of C57BL/6 mice couldn't be induced by different concentration of *C.difficile* bacterial suspension. In most cases, infection caused only mild diarrhoea or no symptoms at all. This disadvantage may limit the application of C57BL/6 mice in the study of refractory or recurrent C. difficile infection. In order to evaluate efficacy and safety of new treatments

before they are given to humans, research into CDAD pathophysiology, and elucidate mechanisms of protective immunity, there is an urgent need to establish a better model of CDAD with clinical representation and good stability.
**Aims & Methods: Aims:** The aim of this study was to construct a *C.difficile*–associated disease model with clinical representation and good stability, provide a promising research tool for the infection of *C.difficile*. **Methods:** We choose 3 different commonly used strains of mice (C57BL/6, BABL/c and KM) in this research, all were exposed to multiple antibiotics (kanamycin 0.04 mg/g, gentamicin 0.0035 mg/g, polymyxin, 0.0042 mg/g) metronidazole 0.0215 mg/g, and vancomycin 0.0045 mg/g) for 9 days. One day later, they were given single intraperitoneal injection of clindamycin (10 mg/kg) and then challenged 1 day later with different doses ($10^8$CFU/ml~$10^{10}$CFU/ml) of the most common clinical isolates by gavage, and then the duration and severity of diarrhea, general state of health and pathological changes of colonic tissues were observed. All results were repeated for three times separately.
**Results:** All of the dealed mice developed symptoms of infection, but severity of diarrhea and weight lose differ among the breeds. Typical histologic features of CDAD, including inflammatory reaction, hyperemia and edema were evident in BALB/c mice, and disease severity varied from mild to severe in accordance with the challenge dose, the mortality of the high dose group is 16.7% (n = 12). While various dose of C difficile didn't result in corresponding change in C57BL/6 and KM mice, C57BL/6 mice all developed mild self-limited diarrhea or no diarrhea at all, no deaths occurred; KM mice's symptom severity has a great individual difference between inter-groups.
**Conclusion:** By comparing the symptoms and pathological manifestations of all experimental groups, we found the symptoms of BALB/c mice are more easily managed by changing the challenge dose. Compared with C57BL/6 and KM mice, BALB/c mice can better represent the usual course and spectrum of CDAD in human beings.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1452 A HOSPITAL-BASED STUDY ON RISK FACTORS OF RECURRENT CLOSTRIDIUM DIFFICILE ASSOCIATED DISEASE IN HONG KONG


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**Introduction:** The incidence and severity of *Clostridium difficile* associated disease (CDAD) is increasing worldwide. Up to 35% of patients are complicated by recurrence of CDAD. This increases morbidity and mortality and the disease burden in hospital. Many studies have identified risk factors for the first episode of CDAD. However, risk factors of recurrent CDAD are not well established. Local data are limited.
**Aims & Methods:** Aims The objective of this study is to determine the recurrence rate and identify risk factors associated with recurrence of CDAD. Methods A 30-month multi-centre retrospective cohort study was conducted by recruiting patients diagnosed to have CDAD (both recurrent and non-recurrent) across three hospitals in Hong Kong. Five hundred and seventy five patients suffering from CDAD were recruited. They were then divided into the recurrent group and non-recurrent group.
**Results:** Of 575 patients recruited, sixty five patients developed recurrent CDAD. The recurrence rate was 11.3%. Multivariate logistic regression analysis was performed. Patients taking proton pump inhibitor (PPI) significantly increased the risk of CDAD recurrence (adjusted OR 2.006, 95% CI 1.135 – 3.546, P = 0.017). Taking PPI more than the WHO defined daily dose[1] further increased the risk (adjusted OR 3.573, 95% CI 1.107 – 11.533, P = 0.033). As PPI dosage increased, the adjusted odds of developing recurrent CDAD also increased, from an odds ratio of 1 (reference) to 2.006 for PPI therapy less than or equal to the WHO defined daily dose, and to 3.573 for PPI therapy more than the WHO defined daily dose. Patients who were fed via a NG tube had a significantly higher risk of recurrent CDAD (adjusted OR 2.177, 95% CI 1.237 – 3.834, P = 0.007). Two-fold increase in the risk of recurrence was found in patients with serum albumin level less than 25 g/L (adjusted OR 2.037, 95% CI 1.118 – 3.711, P = 0.020).
**Conclusion:** This study showed that the recurrence rate of CDAD was 11.3%. Several independent risk factors of recurrent CDAD were identified, which included the use of PPI, NG tube feeding and serum albumin level less than 25 g/L. Moreover, PPI use more than the WHO defined daily dose further increased the risk. The incidence and severity of CDAD recurrence is increasing worldwide. Therefore, it is important to identify these risk factors to help us evaluate and improve our current clinical practice. Judicious use of PPI and regular review of the need of NG tube feeding are important measures to prevent recurrence of CDAD. Morbidity, mortality and thus burden on the health-care system might then be reduced.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1453 PLACEBO RESPONDERS IN A RANDOMISED CONTROLLED TRIAL OF RBX2660 FOR RECURRENT C. DIFFICILE INFECTION: PREDICTIVE VALUE OF 16 S RRNA MICROBIOME ANALYSIS


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**Introduction:** Disruption of the gut microbiota has been demonstrated as a risk factor for C. difficile infection (CDI). Novel therapies aim to restore the gut microbiota to its pre-disease state as a protective factor against recurrence. Findings from recent controlled studies of faecal microbiota transplant have raised questions about a placebo response. We explored the potential of 16 s rRNA analysis as a predictive biomarker.
**Aims & Methods:** The objective of this analysis was to determine whether 16 s rRNA analysis could be used as a predictive biomarker in the assessment of the placebo response to a microbiome-based drug targeted at recurrent CDI. PUNCH CD 2 was a randomised placebo controlled study of RBX2660, a microbiota-based drug manufactured from live human-derived microbes and targeted at the prevention of recurrent CDI. Of the 133 patients in the study, a total of 44 patients were randomised to receive 2 doses of placebo. Longitudinal 16 s rRNA analysis was performed on patient stool after the second dose using the Illumina MiSeq platform. The variable region V4 was targeted to identify the operational taxonomic units (OTUs) in each sample. We report the results of the first 20 consecutive patients in the placebo arm.
**Results:** Of the 20 sequenced patients (55% female; mean age: 59.2 years), 8 experienced recurrent CDI symptoms prior to 56 days; 12 patients did not. At baseline, the microbiome profiles of the 20 patients were similar. At 7 and 30 days, OTU analysis showed increased divergence between patients who went on to further recurrence and those who did not. Clostridiales and Enterobacteriales predominated at all time points. Overall OTU analysis demonstrated a slight but non-significant variation between the two groups.
**Conclusion:** In this randomised controlled study of RBX2660 for recurrent CDI, 16 s rRNA analysis was not predictive of which patients receiving placebo had a further recurrence of CDI symptoms and which did not. Further analysis of the entire cohort is needed to determine the possibility of a predictive analytical method.
**Disclosure of Interest:** C. Jones: Employee, Rebiotix Inc., Roseville, MN, USA B. Shannon: Consultant, Rebiotix Inc., Roseville, MN, USA

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### P1454 MECHANISM OF ANTIBIOTIC-ASSOCIATED DIARRHEA: INSIGHT INTO COLONIC WATER AND ION TRANSPORT, MUCUS SECRETION


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**Introduction:** Diarrhea is the most common side effect of broad-spectrum antibiotic's treatment, which occurs in 5 to 62% cases. Most cases of antibiotic-associated diarrhea (AAD) can be classified in two categories: 1) *Clostridium difficile*- induced diarrhea; 2) idiopathic diarrhea - no infection agent is recognized. The mechanism of idiopathic AAD is not clear.
**Aims & Methods:** The present study was designed to test the hypothesize whether the disturbance in microflora composition after 5 or 14 days ceftriaxone treatment alters colonic water/electrolyte transport and whether this effect is dependent on changes in expression pattern of CFTR, AQP8, ENaC and NHE3 transporters and levels of mucus secretion. Male Wistar rats were treated daily with ceftriaxone (50 mg/kg, i.m.) for 5 or 14 days. Net water and ion transport (Na+, K+, Cl-) were evaluated on the 6th or 15th day by isolated colonic loop perfusion technique in vivo; mRNA expression - by RT-PCR; level of surface colonic mucus layer - by periodic acid/Schiff (PAS) staining; the fecal microflora composition - by bacteriological culture methods; C. difficile toxins A and B - by immunochromatographic assay.

**Results:** We showed that after 5 and 14 days of ceftriaxone administration diarrhea developed in 13% and 6% animals, respectively. While, there were none C. difficile toxins A and B positive rats after 5 days of ceftriaxone administration, but 25% (1 of the 4) animals were positive after 14 days. We have observed pro-secretory changes in colon after 5 days of ceftriaxone treatment. It was associated with downregulation of ENaC expression which are responsible for active sodium absorption and increase CFTR expression which are responsible for active Cl secretion. Moreover, expression of AQP8 was also decreased. After 14 days of ceftriaxone treatment, we have still observed pro-secretory changes in colonic epithelium but less profound than after 5 days of treatment. It has been mainly driven by $Cl^-$ secretion. Expression of CFTR channels was also increased. Surprisingly, that along with net $Cl^-$ secretion, net $Na^+$ absorption was increased as well as expression of electroneutral $Na^+/H+$ exchanger (NHE3) and electrogenic ENaC. Ceftriaxone treatment for 5 days was associated with 3.1-fold ($p < 0.01$) decrease in colonic mucus secretion. After 14 days of ceftriaxone treatment, we observed 3-fold increase in colonic mucus secretion ($p < 0.05$ vs. water treated-rats). These changes were accompanied by increased number of conditionally pathogenic microflora after 5 days treatment and returned to control value after 14 days treatment.
**Conclusion:** The present study demonstrated for the first time that parenteral treatment with cephalosporin antibiotic ceftriaxone had induced diarrhea which was associated with changes in colonic net water and ion transport; allowed us to speculate that clinically observed transitory diarrhea during antibiotic therapy might be physiological defense response driven by shift in normal microflora composition.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1455 ENDOSCOPIC BAND LIGATION (EBL) METHOD USING SMALL-CALIBER COLONOSCOPE FOR COLONIC DIVERTICULAR BLEEDING

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**Introduction:** Incidence of colonic diverticular bleeding has increased in recent years. In colonic diverticular bleeding, the source of bleeding is often difficult to identify. Our hospital had reported that the use of enhanced computed tomography can help improve the bleeding source identification rate1). In recent years, it has been reported that, of hemostasis methods, endoscopic band ligation (EBL) results in a lower rate of re-bleeding than the clipping method2). As of 2015, EBL has been used as the first choice for hemostasis as much as possible at our hospital. A possible disadvantage of EBL is the fact that it requires re-intubation of a scope. At our hospital, when re-intubation the scope after identifying the source of bleeding, we switch from the initial scope to the PCF-PQ260L (Olympus corporation), which offers a superior insertability with its small caliber and passive bending system.
**Aims & Methods:** We examined the usefulness of EBL using the small-caliber colonoscope. Subjects were comprised of 548 patients who underwent emergency lower gastrointestinal endoscopy for colonic diverticular bleeding at St. Marianna University Hospital between January 2005 and March 2016. For all of the patients who underwent EBL, the source of bleeding was identified, after which the initial scope used was changed to the small-caliber colonoscope, and this was re-intubation to perform hemostasis treatment.Patients were divided into two groups according to the method of hemostasis, i.e. the EBL group and the clipping group. We retrospectively analyzed the treatment outcomes for each groups. In the EBL group, the time required to reach the bleeding source upon re-intubation was also examined.
**Results:** Of the 548 patients, the source of bleeding was identified in 233 patients (42.5%). The EBL group had 40 patients, including 25 male and 15 female patients with an average age of $77 \pm 10$ years. The clipping group had 193 patients, including 143 male and 50 female patients with an average age of $69 \pm 12$ years. Oral antithrombotic agents were administered to significantly more ($P < 0.01$) patients in the EBL group (23 patients; 57%) than the clipping group (68 patients; 35%). The most common source of bleeding was the ascending colon in both groups (EBL group: 23 patients; 57%, clipping group: 124 patients; 64%), and no significant difference was observed. Re-bleeding rate was significantly lower ($P = 0.01$) patients in the EBL group (2 patients; 5%) than in the clipping group (44 patients; 23%). Of the patients who experienced re-bleeding, transcatheter arterial embolization was performed on three patients, and emergency surgery was performed on one patient. Following treatment, there were no perforations observed in either group. The mean procedure time for hemostasis treatment was significantly shorter ($P < 0.01$) in the EBL group ($47 \pm 18$ min) than in the clipping group ($66 \pm 33$ min). In the 23 patients in whom the source of bleeding was in the ascending colon, the average cecal intubation time at the the initial insertion was $12 \pm 5$ min, then the mean time to reach the source of bleeding upon re-intubation of the scope was $6 \pm 3$ mins. Thus, the time of re-intubation was significantly shorter that the initial intubation time ($P < 0.01$).
**Conclusion:** Compared to the clipping method, the EBL method resulted in a significantly lower rate of re-bleeding and better hemostasis outcomes. Furthermore, no adverse events occurred. The small-caliber colonoscope gives it superior insertability and allows for shorter re-intubation than the initial intubation time. Furthermore, even with the addition of re-intubation time, the duration of time to achieve hemostasis was significantly shorter with the EBL method than the clipping method. Therefore, these results demonstrated the usefulness of the EBL method with the small-caliber colonoscope.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1456 FECAL MICROBIOTA TRANSPLANTATION – AN OLD TOOL OPENING A NEW ERA IN THE TREATMENT OF CLOSTRIDIUM DIFFICILE INFECTION

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**Introduction: Introduction:** The incidence of *Clostridium difficile* infection (CDI) assumes epidemic proportions, constituting the leading cause of antibiotic-associated diarrhea.[1–3] Recurrence after the first-line treatment with antibiotics is high.[2] Despite its application in humans being described for about 50 years, fecal microbiota transplantation (FMT) has gained recent popularity as it appears to be a safe and highly effective approach for refractory and recurrent CDI.[1,3]
**Aims & Methods: Objective:** This case series aimed to evaluate the efficacy and safety of FMT in the treatment of refractory and recurrent CDI. **Methods:** Between June/2014-February/2015, a prospectively recorded single-centre case series of patients with refractory or recurrent CDI treated with FMT was collected. Primary and secondary outcomes were defined as resolution of diarrhea without recurrence of CDI within 2 months after one or more FMT, respectively.
**Results: Results:** 18 FMT were performed in 14 patients, 64.3 (n = 9) were women with a median age of 72 years. The indications for FMT were refractory CDI in 9 procedures and recurrent CDI in 9. FMT was performed via upper endoscopy in 14(77.8%) procedures and colonoscopy in 4(22.2%). One upper FMT was excluded due to recurrence of CDI after antibiotic exposure for a respiratory infection. The overall cure rate of FMT was 84.6% (11/13) via the upper route and 100% (4/4) via the lower route, with 2 of these lower FMT corresponding to the 2 patients where the upper FMT failed. Primary and secondary cure rates were achieved in 94.1% (16/17) and 100% (17/17) of patients, respectively. No complications were reported during follow-up.
**Conclusion:** FMT appears to constitute a safe and effective approach in the management of refractory and recurrent CDI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1457 FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION: TRANSPLANT PROTOCOL BY ENEMA AND PRELIMINARY RESULTS

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**Introduction:** Fecal microbiota transplantation (FMT) is a safe and effective approach in the management for refractory and recurrent Clostridum difficile infection (R-CDI). Administration of fecal samples can be performed via lower gastrointestinal (GI) route as colonoscopy or enema or via upper GI route, including nasogastric tube and gastroduodenoscopy. The retention enema is an excellent option but is may be difficult for some patients to retain the transplanted stool and more infusions may be required.
**Aims & Methods:** The aim of the study was to determine the efficacy of FMT via enema with an alternative procedure. Fecal transplant protocol: We included patients who were at least 18 years of age with a R-CDI. Exclusion criteria were prolonged compromised immunity because of recent chemotherapy, the presence of human immunodeficiency virus (HIV) infection, or prolonged use of prednisolone at a dose of at least 60 mg per day; pregnancy; use of antibiotics other than for treatment of C. difficile infection at baseline. Patients received an abbreviated regimen of vancomycin (500 mg orally four times per day for 4 or 5 days); polyethylene glycol-based colonoscopy preparation on the day prior to FMT, loperamide, 2 or 3 hours prior the infusion, for the retention of transplanted material. Donors and fecal samples preparation Fecal samples were

collected by five volunteers donors ( < 30 years of age). The feces were screened for parasites, *C.difficile*, and enteropathogenic bacteria. Blood was screened for antibodies to HIV; hepatitis A, B, and C; cytomegalovirus; Epstein–Barr virus; Treponema pallidum; Strongyloides stercoralis; and Entamoeba histolytica. Donor fecal samples (50 g) were mixed with 250 or 500 ml of sterile saline buffer, mixed into slurry and filtered once with surgical gauze for large particles and twice with a coffee filter. If the transplant was not performed the same day of sample collection, the solution was frozen in 10% (vol/vol) glycerol and stored at −80°C, according to standard procedure. Patients were randomly allocated to receive frozen or fresh FMT via enema. The fecal solution was administreted using a suction catheter (16 fr). Before the infusion, a rectal balloon (has been used a standard Foley catheter, 20 fr) was inflated with sterile saline solution up to 20–30 mL volume distension. This procedure allowed to avoid significant loss of fecal samples during infusion.

**Results:** Eleven procedure were perfomed in eight patients. The average patient age was 69 years (range, 42–83 years). Follow-up ranged from 10 days to 1 years. The patients received a 250-ml suspension on 75% of cases (range 250–500 mL). The time of infusion was average 30 minutes. Heighty-seven percent of patients experienced resolution (7/8) after a single treatment. Only one patient was treated with 3 infusion without response. The resolution of diarrhea occurred in 5/7 patients within 24 hours and in 2 patients after 72 hours from transplantation. No major adverse events correlated to FMT was registered.

**Conclusion:** Our preliminary results confirmed the efficacy of FMT by enema using a retention rectal balloon. The procedure has been well accepted and tolerated by patients without any complications. The healing has been immediate in the majority of patients with short recovery time.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1458 FECAL MICROBIOTA TRANSPLANTATION VIA ENEMA FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION MODULATES THE INFLAMMATORY HOST RESPONSE AND RESTORE INTESTINAL DYSBIOSIS

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**Introduction:** Fecal microbiota transplantation (FMT) is able to restore resistance to *C.difficile* (CD) colonizationby re-establishing a healthy microbial ecosystem in the gut of patients with high cure rates. Inaddition to A/B toxins effect, recent study showed that the host immune response and microbiotacomposition play a role in the pathogenesis of CD infection.

**Aims & Methods:** The aim of the study was to determinethe efficacy of FMT via enema in recurrent CD infection (R-CDI) and to evaluate the FMT impacton the host immune response and the gut microbiota composition. Methods. Fecal transplant protocol. The study recruited patients with R-CDI admitted at the Policlinico Umberto I Hospital, (Rome).Patients received 4–5 days oral vancomycin (500 mg every 6 hours) and the day prior to FMT, polyethylene glycol-based oral lavage of the colon. Loperamide was given 3 hours prior to the infusion in order to facilitate the retention of transplanted material. Fecal material was collected from 5 healthy donors (<30 years old). Patients were randomly allocated to receive frozen or freshFMT via enema. Microbiota characterization. Fecal microbiota composition was evaluated before and after the FMT in patients and healthy donors. To this purpose, 16 S rDNA sequencing (MiSeq) was used for fecal microbiota characterization. The real Time PCR was employed for a quick evaluation of the fecal ecosystem by analyzing the relative abundance of the bacterial phylum *Bacteroitedes* and *Firmicutes*, and of the bacterial species Escherichia coli and Fecalibacterium prausntizii, whose ratio was used as a dysbiosis index. T cells phenotype Lymphocyte surface phenotypes were evaluated in 4 patients by flow cytometry using freshperipheral blood before (T0) and after (T1) FMT. For the activation analysis of T cells CD4+ andCD8+, the following fluorochrome-labeled antibodies were used: Pacific Blue-CD3, PerCp/Cy5.5- HLA DR, Pe/Cy7-CD8, CD38-APC, APC/Cy7-CD4. Immune activation was defined as co- expression of HLADR +CD38 + on CD 4 and CD8 T cells.

**Results:** A total of 11 FMT procedures were performed in eight patients. The median patients age was 69 years (range 42–83 years). Seven patients (87%) experienced resolution; among them, 6/7 (85.7%) were cured after a single treatment. No major adverse events were observed. Microbiota characterization. Before FMT, the phylum of *Proteobacteria* was highly prevalent in all patients, in particular the gamma *Proteobacteria* class and the Enterobacteriaceae family. After the FMT, a rapid decrease of the *Proteobacteria* was observed, with a parallel increase of the phyla *Firmicutes* and Bacteroitedes, which reached 80% of the total microbiota.Immuneractivation. At T0, high levels of CD4 + and CD8 + HLADR + CD38 + T lymphocytes were found. The levels of immuneractivation of T lymphocytes were decreased after FMT, but this variation was not statistically significant.

**Conclusion:** FMT via enema was effective, safe and induced a rapid recovery of the microbiota balance with a reduction of the inflammatory response.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1459 REPEAT FECAL MICROBIOTA TRANSPLANTATION BY COLONOSCOPY FOR CLOSTRIDIUM DIFFICILE-ASSOCIATED PSEUDOMEMBRANOUS COLITIS: RESULTS FROM A PROSPECTIVE, SINGLE-CENTRE COHORT

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**Introduction:** Fecal microbiota transplantation (FMT) from healthy donors is highly effective for the management of recurrent *Clostridium difficile* infection (rCDI). Although with minor evidence, FMT appears to be a reliable treatment of severe CDI. C-difficile associated pseudomembranous colitis (PMC) is an endoscopic sign of severe disease, potentially life-threatening. In our recently published randomized controlled trial,[1] we observed that repeat FMT by colonoscopy was able to cure PMC associated to rCDI.

**Aims & Methods:** Our aim was to describe a prospective series of patients with rCDI-associated PMC treated with repeat FMT by colonoscopy at our Centre. We identified prospectively all patients with rCDI and endoscopic appearance of PMC treated with FMT by colonoscopy. We excluded the first two patients from the analysis, as the treatment protocol had still not defined when we treated them Demographic and clinical data of included patients, together with their endoscopic and FMT-related characteristics, were collected. At first infusion, patients underwent the following protocol, previously described[1]: a short regimen of vancomycin (125 mg by mouth four times a day for 3 days), followed by bowel cleaning with 4 L of macrogol preparation (SELG ESSE) on the last 1 or 2 days (according to the clinical condition of the patients) of antibiotic treatment, followed by FMT from healthy donor by colonoscopy the next day. Patients received further infusions after being restricted to a light diet and prepared for colonoscopy by taking only 2 L of bowel prep before the colonoscopy, until the resolution of colitis.

**Results:** Overall, we included for the analysis 10 patients with rCDI-associated PMC treated with repeat FMT; of them, 8 were inpatients (80%). Mean age was 73 years old (range: 60–89). Female patients were 7 (70%). The mean number or CDI recurrences was 3. In all treated patients, we observed the progressive disappearance of pseudomembranes as we repeated the infusions. On average, patients received 3 fecal infusions (range: 2–4). Infusions were delivered between 3 and 6 days after the first FMT. At first colonoscopy, pseudomembranes were identified in the whole colon in 5 patients (50%), and in the left/distal colon in the other 5 (50%), respectively, although in two patients we delivered the fecal material in the left colon, without completing the colonoscopic exam, because of severe inflammation, which disappeared after further infusions. Overall, both fresh and frozen material, as well as both external and related donors, were used for FMT. Repeat FMT cured rCDI-associated PMC in all patients (100%). No serious adverse events related to the procedure were observed.

**Conclusion:** Repeat FMT achieved a 100% resolution rate of rCDI-associated PMC in our small prospective series. As PMC is a sign of severe, potentially life-threatening disease, its endoscopic recognition is of paramount importance, and its treatment through colonoscopic FMT appears to be highly effective. Therefore, both further research and dissemination of this technique are warranted for a better management of patients with rCDI-associated PMC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1460 A PROSPECTIVE STUDY ON THE INCIDENCE AND RISK FACTORS FOR NOSOCOMIAL CLOSTRIDIUM DIFFICILE INFECTION

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**Introduction:** *Clostridium difficile* infection (CDI) is an increasingly important nosocomial problem complicating up to 1.0% of all hospital admissions and associated with considerable health burden

**Aims & Methods:** To determine the incidence, risk factors and outcomes of nosocomial CDI in a major University Medical Center in Lebanon. In this

two-year ongoing prospective study, nosocomial CDI attack rates were measured, and relevant patient information was collected including baseline characteristics, antibiotic and PPI use, length of stay, morbidity and mortality. Patients were followed for 8 weeks after discharge for relapsing CDI identified by recurrent symptoms ± positive toxin or nucleic acid testing. Stool samples were collected for ribotyping and genotyping of C. difficile strains.
**Results:** Over the study period, 177 patients were diagnosed with nosocomial CDI for an incidence of 0.20% (177 of 86,564 hospital admissions). Of those, 163 patients (mean age 62.2 ± 19.1 years) gave informed consent and constitute the study population for this interim analysis. Mean hospital stay was 23.8 ± 30.1 days (range 0–278). Infection was diagnosed within 7 days of admission (range 0–95 days) in 103 patients (63.6%). Patients had no history of prior CDI but 110 of the 163 (67.5%) were hospitalized within 12 weeks of the index admission. 38 (23.3%) had received prior antibiotics (mostly fluoroquinolones) within 8 weeks before hospitalization. 23.9% of inpatients who developed CDI did not receive antibiotics during their current hospital stay prior to diagnosis. The study cohort had considerable comorbidities evidenced by a Charleston Comorbidity Index (CCI) ≥ 8 in 30.1% of patients. Carbapenems (50.1%) and piperacillin-tazobactam (41.1%) were the most commonly used in-hospital antibiotics. PPI use was frequent, both at home (52.1%) and during hospitalization (86.5%). CDI relapse occurred in 36 patients (22.1%). There was a significant association between prior hospitalization and CDI recurrence within 60 days of discharge ($p = 0.02$). No significant associations were found between relapse and age, PPI use, CKD, immune compromised status, or CCI (< or ≥8). Mortality occurred in 14.7% of patients. On logistic regression, only a CCI ≥8 was significantly associated with mortality [OR 4.392 (1.363–14.149); $p = 0.013$]. Bacterial ribotyping and genotyping studies are in progress.
**Conclusion:** Antibiotic exposure, comorbidities, and prior hospitalization constitute the major risk factors for nosocomial CDI. Relapse is relatively common and is associated with repeat hospitalization. High baseline comorbidity score was the only predictor of increased mortality.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1461 OBESITY, DIABETES MELLITUS, HEAVY ALCOHOL CONSUMPTION, SMOKING AND RISK FOR COLORECTAL POLYPS AND CANCER IN A FIT-POSITIVE SCREENING POPULATION

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**Introduction:** Colorectal cancer (CRC) is one of the leading causes of cancer incidence and death worldwide. Epidemiological studies obtained from several world areas have shown that obesity and type 2 diabetes increase the risk for the disease. Obesity is the fastest growing risk factor, and its incidence has increased by 1% every year, including Southern Europe. Thus, it could represent an important risk factor also in this area.
**Aims & Methods:** To evaluate the association between comorbidities and lifestyle factors including obesity, diabetes mellitus, alcohol use, smoking and risk for colorectal cancer and adenoma/serrated polyps (excluding hyperplastic polyps) in the population aged 50–75 years who were part of a FIT-based colorectal cancer screening program in Northern Italy. Between March 2005 and December 2013 a total of 3906 FIT + subjects underwent total colonoscopy. We compared subjects without lesions with those with polyps (adenomas and/or serrated), and also with colorectal cancers. Heavy drinkers were considered those with alcohol consumption of > 35 gr/daily. Smokers were considered those who either claimed to have smoked throughout their life at least 100 cigarettes and to be a smoker at the time of interview, or to have quit less than 10 years prior to undergoing screening. Obese subjects were considered those with a BMI ≥ 30 $Kg/m^2$. A multivariate logistic regression analysis was used to estimate odds ratios.
**Results:** Of the patients undergoing colonoscopy, 1903 subjects had a diagnosis of at least one adenoma or serrated polyp. Two hundred and fifty-two subjects (6.5%) were diagnosed with colorectal cancer (195 colon and 56 rectum). Obesity, heavy drinking and smoking were significantly associated with an increased risk of adenomatous/serrated polyps, and colorectal cancer. For adenomatous/serrated polyps odds ratios were 1.40 (95% CI, 1.15–1.69) for obese individuals, 1.05 (95% CI, 0.67–1.65) for heavy alcohol drinkers and 1.44 (95% CI, 1.25–1.67) for smokers, respectively. For patients with colorectal cancer, odds ratios were 1.20 (95% CI, 0.83–1.75) for obese subjects, 3.05 (1.63–5.72) for heavy drinkers, 1.30 (95% CI, 0.97–1.75) for smokers, 1.38 (95% CI, 0.88–2.17) for individuals with type 2 diabetes, respectively. When considering colon cancer alone, odds ratios were 1.52 (95% CI, 1.01–2.29) for obese subjects, 3.54 (95% CI, 1.83–6.85) for drinkers, 1.26 (95% CI, 0.90–1.76) for smokers, 1.42 (95% CI, 0.87–2.32) for subjects with type 2 diabetes, respectively.
**Conclusion:** In our FIT+ population, obesity, heavy alcohol consumption and smoking are significant risk factors for adenomas/serrated polyps and colorectal cancers. Diabetes mellitus has an independent relationship with CRC that is more significant for cancer of the colon than the rectum. In the future, early screening strategies should be targeted to high-risk individuals, in particular to those with obesity and type II diabetes.
**Disclosure of Interest:** L. Ricciardiello: Received an unrestricted research grant from SLA Pharma UK
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## P1462 PREVALENCE OF SERRATED POLYPOSIS SYNDROME IN A FIT-BASED COLORECTAL CANCER SCREENING COHORT IN ITALY

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**Introduction:** According to the WHO definition, Serrated Polyposis Syndrome (SPS) is a disease characterized by either 1) the presence of at least five serrated polyps proximal to the sigmoid colon with two ≥10 mm in size, 2) more than 20 serrated polyps throughout the colon, or 3) any number of serrated polyps proximal to the sigmoid colon in an individual who has a first-degree relative with SPS. While SPS demonstrates hallmarks of a genetic disease, the exact risk for colorectal cancer (CRC) is unknown, although a cumulative 7% risk of CRC at 5 years in patients under surveillance was reported[1]. No data on SPS are available among the Italian population. Thus, the aim of our study was to assess the prevalence of SPS in a FIT-based CRC screening population in Italy, and possible associations with comorbidities and lifestyle factors.
**Aims & Methods:** We retrospectively reviewed records of 3906 FIT-positive patients aged 50–75 participating to a CRC screening program in North Italy between March 2005 and December 2013. For each patient we extracted endoscopic and pathological reports, age at the time of colonoscopy, gender, BMI, comorbidities and lifestyle information including cigarette smoking, alcohol consumption, and compared them with subjects with negative colonoscopies. Mann-Whitney and Fisher's exact tests were used to test quantitative variables and proportions, respectively.
**Results:** Of the 3906 patients reviewed, 12 (0.31%) met the WHO criteria for SPS. Of them, 75% (9/12) were diagnosed at first colonoscopy. 83% (10/12) of patients fulfilled WHO criterion number 1, and 16.7% (2/12) patients fulfilled WHO criterion number 2. Mean age at diagnosis was 60.5 years. 41.6% (5/12) of patients presented synchronous adenomatous polyps, and in 4/5 patients the adenomas had advanced features. When comparing SPS patients to those with a negative colonoscopy, we found a strong correlation with smoking (66% vs 25%, $p = 0.004$) and a borderline association with BMI ≥ 25 (83% vs. 57%, $p = 0.058$).
**Conclusion:** Our data are in line with those obtained from other European cohorts[2], indicating that SPS is more common than previously thought. SPS was strongly associated with smoking, and a borderline association was found with being at least overweight. Our data suggest that lifestyle factors might be important contributors to the onset of SPS.
**Disclosure of Interest:** L. Ricciardiello: Unrestricted research grant by SLA Pharma UK
All other authors have declared no conflicts of interest.

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## P1463 RECURRENT ADVANCED COLONIC NEOPLASIA AFTER POLYPECTOMY ON SURVEILLANCE COLONOSCOPY ACCORDING TO RISK GROUPS AND AGE GROUPS: A RETROSPECTIVE STUDY OF 1,974 ASYMPTOMATIC KOREANS

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**Introduction:** The incidence of colorectal cancer in Korea is increasing. The age-standardized mortality rates of colorectal cancer continue to increase, unlike those of other common cancers whose mortality rates have decreased in recent years.[1] As the prevalence of advanced adenoma and the incidence of colorectal cancer increases with age, advanced adenoma, which has been implicated in the etiology of colon cancer, is a significant concern for the average-risk individual.
**Aims & Methods:** This study aimed to estimate the cumulative incidence of recurrent advanced colonic neoplasia after polypectomy on surveillance follow-up colonoscopy, and compare the differences according to risk groups and age groups. We reviewed 9,102 subjects who underwent screening colonoscopy, and we retrospectively analyzed 1,974 subjects who underwent follow-up surveillance colonoscopy after polypectomy. We estimated the cumulative incidence for recurrent advanced colonic neoplasia (advanced adenoma or adenocarcinoma) according to baseline risk groups: high-risk group (advanced adenoma or ≥3

adenomas), low-risk group (1–2 adenomas < 1 cm in size), and normal group. The rate of recurrent advanced colonic neoplasia was compared among age groups (50 s, 60 s, and more than 70 years). The relative risk was computed by the hazard ratio using Cox proportional regression after multivariate (age group, sex, family history of colorectal cancer, smoking status, BMI > 25 kg/m$^2$, FOBT (fecal occult blood test) positivity, 3 or more adenomas, colonic adenoma ≥1 cm in size, villous component, and risk groups) adjustments.
**Results:** At screening colonoscopy, subjects' mean age was 55.9 years (55.7%, men). Among 9,102 subjects, 3,431 (37.7%) had a colonic adenoma. 464 subjects (5.1%) had advanced adenoma. Forty-five subjects had an adenocarcinoma on screening colonoscopy (0.49%). After polypectomy, 1,974 subjects (men 72.1%) underwent follow-up surveillance colonoscopy. The mean follow-up period was 41.8 months. 111 advanced neoplastic tumors were newly diagnosed during follow-up surveillance colonoscopy. Among the 111 advanced neoplasia, 58 subjects (52.3%) had three or more adenomas, 96 (86.5%) had a colonic neoplasia ≥1 cm in size, and 23 (20.7%) had a villous histology. No significant difference was observed in the location of recurrent advanced neoplasia between the right-sided colon (62.2%) and left-sided colon (37.8%) (P = 0.219). Six adenocarcinomas from 6 subjects were newly diagnosed during follow-up surveillance colonoscopy. The 5-year cumulative incidence rates of advanced neoplasia by risk groups were 20.5% in the high-risk group (95% CI 0.73 to 0.86), 7.8% in the low-risk group (95% CI 0.90 to 0.95), and 2.2% in the normal group (95% CI 0.96 to 0.99) (P < 0.001). The 3-year cumulative incidence rates of advanced neoplasia were 9.3% in the high-risk group (95% CI 0.87 to 0.94), 3.1% in the low-risk group (95% CI 0.96 to 0.98), and 0.6% in the normal group (95% CI 0.99 to 1.0) (P < 0.001). The 5-year cumulative incidence rates of advanced neoplasia by age groups were 6.8% for 50 s (95% CI 0.91 to 0.96), 10.1% for 60 s (95% CI 0.86 to 0.94), and 20.0% for aged ≥70 years (95% CI 0.69 to 0.92) (P < 0.001). The 3-year cumulative incidence rates of advanced neoplasia were 2.9% for those 50 s (95% CI 0.96 to 0.98), 4.7% for 60 s (95% CI 0.93 to 0.98), and 10.1% for aged ≥70 years (95% CI 0.83 to 0.97) (P = 0.001). In multivariate analysis (adjusted for age group, sex, family history of CRC, smoking status, BMI > 25 kg/m$^2$, FOBT positivity, 3 or more adenomas, colonic adenoma ≥1 cm in size, villous component, and risk groups), the high-risk group (vs. low-risk group, HR = 7.5, 95% CI 2.0 to 27.8) (P = 0.003) and age ≥ 70 years (vs. 50 s, HR = 4.1, 95% CI 1.7 to 9.8) (P = 0.002) were significant risk factors for recurrent advanced neoplasia after polypectomy.
**Conclusion:** The high-risk group and age older than 70 years were significant risk factors for advanced neoplasia recurrence on surveillance colonoscopy after polypectomy or adenoma removal in average-risk individuals.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1464 EVALUATION OF A 25-GENE PANEL IN PATIENTS WITH SUSPECTED LYNCH SYNDROME: FAMOSA STUDY

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**Introduction:** The role of multigene panels for hereditary cancer risk assessment is yet to be established. We aimed at describing the prevalence of cancer predisposition gene mutations identified by a multigene panel in individuals with suspected Lynch syndrome (LS).
**Aims & Methods:** We performed germline analysis with a next-generation sequencing 25-gene-panel (Myriad myRisk™ Hereditary Cancer) using DNA from 95 patients with suspected LS (endometrial cancer < 50 y-o and/or fulfillment of revised Bethesda criteria) from Nov-2014 through March-2015 within the FAMOSA study. We classified all identified germline variants for pathogenicity and calculated the prevalence of pathogenic mutations and variants of uncertain clinical significance (VUS). We analyzed data on patients' personal and family history of cancer.
**Results:** We included 95 patients [female:46(48.5%), mean age:48.6+12]: 8(8.5%) with endometrial cancer and 87(91.5%) with colorectal cancer. Multigene panel testing identified 20(21%) patients with LS syndrome mutations (8MLH1, 7MSH2, 4MSH6, 1PMS2) and 1(1%) with a mutation in BRCA2 in a 35 y-o woman without personal/familial history of breast/ovarian cancer. In patients diagnosed with mutations in the MMR genes and prior molecular screening (n = 9), two displayed MMR proficiency and 5 patients had a negative prior genetic result by conventional techniques.
**Conclusion:** In individuals with suspected Lynch syndrome, multigene panel testing identified unexpected high-penetrance mutations in 1% of cases. Parallel sequencing also detected a meaningful number of cases with previous false negative results
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1465 NEGATIVE TEST RESULTS OF FECAL IMMUNOCHEMICAL TEST IN PRE-TESTED COLORECTAL CANCER PATIENTS

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**Introduction:** **B**urgenland **PRE**vention trial of colorectal cancer **D**isease with **I**mmunologi**C**al **T**esting (B-PREDICT) aims to reduce colorectal cancer (CRC) incidence. All inhabitants of Burgenland aged between 40 and 80 years are included in annual fecal immunochemical test (FIT)-based screening. FIT positive tested individuals were subjected to colonoscopy. Recently, test results of 12 years screening were evaluated. We evaluated the difference between annually and biannually FIT testing.
**Aims & Methods:** B-PREDICT, initiated in 2003 was expanded to the whole province Burgenland in 2006. Annually, more than 150,000 individuals aged between 40 and 80 years are invited to participate in FIT screening. In total, 1,400,000 stool sample containers were delivered to the target group and 547,672 used sample containers were returned to general practitioners, reflecting a participation rate of 39.1%. A qualitative assay was used until 2009, that was replaced by a quantitative system (OC-Sensor, Mast Diagnostica, Germany, cut-off 50 ng Hb/mL) by beginning of 2010. In total, 2,160 patients with initial diagnosis (ID) of CRC were recorded during the period of observation. 1,301 colonoscopies, performed within 30 days before ID were analyzed in regard of indication for colonoscopy. FIT results within the same year, one year and two years prior to ID of CRC were analyzed in pre-tested patients comparing different test systems.
**Results:** In total, 22% of all test results within the year of ID were false negative, 55% within one year and 72% within two years prior to ID. False negative results of the qualitative quick test were 20% in the same year, 59% for 1 year and 73% for 2 years before ID, respectively. For quantitative OC-Sensor, 23% of test results were false negative in the year of ID, 46% within 1 year and 65% within 2 years before ID. The distributions of negative test results of different test systems showed no significant differences.
**Conclusion:** Efficacies of different test systems are comparable. However, rates of false negative results evaluated in pre-tested CRC patients are still high. Thus, annually stool testing may be beneficial.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1466 TUMOUR SPECTRUM OF LYNCH SYNDROME IN A PORTUGUESE POPULATION

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**Introduction:** Accurate determination of tumour spectrum in Lynch syndrome (LS) patients and estimation of its relative risk (RR) is essential for counselling and establishing appropriate surveillance programs.
**Aims & Methods:** We aimed to characterize tumours presented in a Portuguese population with LS and to estimate the RR of each tumour comparing with the general population. We included LS families followed in a specialized centre between 1996–2014. We collected demographic data, tumour type and gene mutations. To calculate tumour RR we used a reference cohort from the Portuguese Oncologic National Registry. Statistical analysis: SPSS v22.
**Results:** Of 112 LS families (MSH2 gene mutations - 61% / MLH1–32% / MSH6–6% / PMS2–0.8%) we identified 377 mutation carriers (MC) with

57% female. Overall there were 344 tumours recorded in 54% of MC: 58% colorectal cancer (CRC) and 42% extracolonic tumours (ECT). Men had more CRC ($p = 0.038$), whereas women had more ECT ($p = 0.001$). Mean age at diagnosis was lower for CRC ($p < 0.001$). MLH1 mutation carriers had a higher frequency of CRC ($p = 0.034$); MSH2 MC had a higher frequency of urothelial cancer ($p = 0.038$) and a tendency for prostate cancer ($p = 0.054$); and in MSH6 MC there was a tendency to higher frequency of ovarian cancer ($p = 0.066$). ECT considered part of LS spectrum: endometrial cancer (12%), ovarian (5%), stomach (4%), urothelial (4%), small bowel (3%), pancreas (0.6%), cholangiocarcinoma (0.3%) and sebaceous tumours / keratoacanthomas (3%). Non-LS spectrum tumours: other skin cancers (3%), prostate (2%), breast (1%) and others (3%). In our population, we found an increased RR for skin tumours (RR 73.17; 95% CI 47.02–109) and cancers of the small bowel (RR 45.44; 95% CI 25.27–75.75), renal pelvis/ureter (RR 41.34; 95% CI 20.16–75.87), endometrium (RR 17.4; 95% CI 12.65–23.37), ovary (RR 15.64; 95% CI 9.26–24.86), colon/rectum (RR 13.58; 95% CI 11.78–15.57) and stomach (RR 2.598; 95% CI 1.51–4.19).

**Conclusion:** To the best of our knowledge, this is the first report of the tumours presented and their RR in a significant number of Portuguese families with LS. We confirmed the presence of an elevated risk for LS-spectrum cancers, as previously described in the literature.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1467 EVALUATING 12 YEARS OF FECAL IMMUNOCHEMICAL TEST-BASED COLORECTAL CANCER SCREENING IN BURGENLAND

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**Introduction:** **B**urgenland **PRE**vention trial of colorectal cancer **D**isease with **I**mmunologi**C**al **T**esting (B-PREDICT) aims to reduce colorectal cancer (CRC) incidence. All inhabitants of Burgenland aged between 40 and 80 years are included in annual fecal immunochemical test (FIT)-based screening. FIT positive tested individuals were subjected to colonoscopy. Recently, test results of 12 years screening were evaluated.

**Aims & Methods:** B-PREDICT, initiated in 2003 was expanded to the whole province Burgenland in 2006. Annually, more than 150,000 individuals aged between 40 and 80 years are invited to participate in FIT screening. In total, 1,400,000 stool sample containers were delivered to the target group and 547,672 used sample containers were returned reflecting a participation rate of 39.1%. A qualitative assay was used until 2009, that was replaced by a quantitative system (OC-Sensor, Mast Diagnostica, Germany, cut-off 50 ng hemoglobin/mL) in 2010.

**Results:** Age-standardized CRC incidence in Burgenland was 43.4/100.000 (1998/2000, Statistik Austria) and thereby heading the Austrian cancer statistics. Since implementation of B-PREDICT, incidence rates were continuously reduced to 25.7/100.000 (average 2009/2011). In total, 2,160 patients with initial diagnosis (ID) of CRC were recorded during the observation period. 1,301 colonoscopies, performed within 30 days before ID were analyzed in regard of indication for colonoscopy yielding the following distribution: hematochezia 256, FIT (B-PREDICT) 196, anemia 168, suspected malignancy 127, guaiac test 117, follow-up care after CRC 58 or after polypectomy 54, loss of weight 42, screening colonoscopy 41, obstipation 36, diarrhea 34, abnormal defecation 29, planned polypectomy 14, and others 129. The total number of recorded colonoscopies is 107,796 including 13,590 screening colonoscopies and 21,257 FIT-triggered colonoscopies. CRC detection rates for screening colonoscopy were 0.3% and 0.9% for FIT-triggered colonoscopies.

**Conclusion:** Compared to screnning colonoscopy the CRC detection rate was three times higher when the target group was pre-tested using FIT.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1468 FAMILIAL COLORECTAL CANCER AND GENETIC SUSCEPTIBILITY: A SCREENING OF 99 COLORECTAL RISK GENE VARIANTS IN FIRST DEGREE RELATIVES OF PATIENTS WITH COLORECTAL CANCER

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**Introduction:** Epidemiological studies have reported a 2- to 3-fold increased risk of colorectal cancer (CRC) in first-degree relatives (FDR) of patients with CRC compared with the overall population. Since FDR share 50% of genes with CRC cases, it is likely that susceptibility to CRC in these individuals results from common variants in low-penetrance genes associated with CRC risk. However, very little is known about the prevalence of these CRC risk variants in FDR of patients with CRC.

**Aims & Methods: Aim:** To evaluate potential differences in the distribution of genotypes and allele frequencies of certain single nucleotide polymorphisms (SNPs) associated with CRC risk in FDR of patients with CRC and individuals with no family history of CRC. **Methods:** We carried out a case-control study comprising 750 FDR of patients with non-syndromic CRC (cases), and 750 sex-aged- and histological lesion- matched individuals with no family history of CRC (controls). Cases and controls were selected from the Spanish CRC screening registries in Aragon and The Canary Islands. All subjects underwent at least one colonoscopy and diagnosis was confirmed by histological study. Both, cases and controls, were classified according to histological findings in the following 3 groups: a) individuals with no colorectal lesions, b) subjects with non-advanced adenomas (NAA), and c) subjects with advanced adenomas (AA). Genomic DNA from cases and controls was genotyped for a panel of 99 SNPs previously associated with CRC risk by the MassArray™ (Sequenom) platform. Genetic analysis was performed using the SNPassoc package implemented in R. To address the issue of adjustment for multiple testing, the false discovery rate method and Bonferroni's correction were applied.

**Results:** Average age of participants was $54.5 \pm 9.4$ years with a slight predominance of women (51.7%). In 57% of patients, no preneoplastic lesions were found. By contrast, 288 patients (144 cases and 144 controls) showed NAA, and 354 patients (177 cases and 177 controls) had AA. Concerning gene analysis, and after applying the false discovery rate method, allele A of the rs17094983 intergenic SNP (DACT1-RPL31P4) was found to be significantly less frequent in FDR of patients with CRC than in controls (13.6% vs 17.8%; log-additive model, OR:0.72, 95% CI:0.58–0.89). Moreover, stratified analysis by histological lesions showed additional differences in genotype distribution between cases and controls. Thus, rs647161C variant located in the C5orf66 gene was significantly less frequent in cases than in controls (30.4% vs 37.8%; log-additive model, OR:0.73, 95% CI:0.59–0.89) among patients without preneoplastic lesions. In addition, individuals carrying the rare allele A of the rs11255841 variant in the lncRNA gene LINC00709 were significantly more frequent in the group of cases than in controls (54.3% vs 37.1%; dominant model, OR:2.04, 95% CI:1.19–3.51) among patients with NAA.

**Conclusion:** The specific variants associated with CRC risk rs17094983, rs647161 in C5orf6, and rs11255841 in LINC00709 genes show significant differences in genotype distribution between FDR of patients with CRC and individuals with no family history of CRC. Our results suggest the involvement of these variants in the genetic susceptibility to familiar CRC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1470 MUTYH MUTATIONS IN PATIENTS WITH EARLY-ONSET COLORECTAL CANCER – PRELIMINARY RESULTS

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**Introduction:** Early-onset (≤50 years) colorectal cancer (CRC) is suggestive of a hereditary predisposition that may have important consequences for the index case and their relatives. Lynch syndrome, which is caused by germline mutations in DNA mismatch repair (MMR) genes, is thought to account for up to 20% of early-onset CRC. Thus, the majority of early-onset CRC has proficient MMR genes and a yet unidentified genetic predisposition. Population-based studies have suggested that MUTYH mutations can fill the molecular diagnostic gap in this group of patients.

**Aims & Methods:** The objective of our study was to evaluate the contribution of germline MUTYH gene mutations in patients with early-onset CRC. We evaluated patients with early-onset CRC referred to a Specialized Consultation and recorded clinical and demographic data. Both microsatellite instability (IMS), MS-S: stable; MS-L: low; MS-H: high), and immunohistochemistry analysis were performed in tumours. Mutational analysis in MUTYH gene was performed by NGS/MLPA and variants were confirmed by Sanger sequence.

**Results:** So far, a total of 38 patients (male $n = 16$) were analyzed, mean age of 40 years (23–50), with CRC in the right colon ($n = 10$), left colon ($n = 14$), rectum ($n = 14$) in stage in I ($n = 4$), II ($n = 8$), III ($n = 19$) and IV ($n = 7$); 34% with synchronous or metachronous adenomas, being serrated lesions in 4; 13% and 24% had family history of CRC or adenomas, respectively, and 18% had family history of extra-colonic cancers. IMS: IMS-S $n = 27$, IMS-H $n = 4$, IMS-L $n = 2$, not available $n = 5$. In IMS-H tumours there was loss of expression of MLH1/PMS2, however, it was not documented any pathogenic germline mutation in MMR genes. We did not find biallelic MUTYH mutations in none of the 38 patients. However, we found monoallelic mutations in 2 (5%) patients, in the hotspot G396D. These 2 patients had an IMS-S CRC diagnosed at 37 and 39 years, the first one with personal and family history of adenomas.

**Conclusion:** These results, although preliminary, suggest that biallelic mutations are not responsible for a significant percentage of early-onset CRC. However, the high prevalence of monoallelic mutations in this population may justify an increased risk for adenomas / CRC.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1471 PROGNOSIS AND CHEMOSENSITIVITY OF COLORECTAL CANCER ARE ASSOCIATED WITH CHANGES IN MICROTUBULES COMPOSITION

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**Introduction:** It is known that the expression of beta-tubulin isotypes is changed in cancer but there is still not enough data about such alterations in colorectal cancer (CRC) and their impact on prognosis and chemosensitivity.

**Aims & Methods:** The objective of this study was to reveal influence of changes in the level of betaI- and betaIII- isotypes of tubulin on CRC outcome. The study was performed on surgical histological material of 125 colorectal adenocarcinomas from 124 patients. Double immunofluorescence with anti-cytokeratin antibody and anti-betaI- or anti-betaIII-tubulin was performed. The level of the betaI-tubulin expression was analyzed by image analyses software: epithelial regions were automatically selected by cytokeratin channel; acquired regions of interest have been used as a mask of selection on tubulin channel; integrated density and area of regions of interest were measured. Expression value was calculated as ratio of integrated density to epithelial region's area and then normalized according to positive and negative controls.

**Results:** The expression of betaI-tubulin was significantly elevated in CRC (median 36.6 in normal mucosa vs. 78.8 in CRC, $p = 0.000$). Moreover, normalized value of betaI-tubulin expression in CRC less then 85.1 and 71.5 was associated with lower disease-free ($p = 0.008$) and cancer-specific survival ($p = 0.015$) respectively. BetaIII-tubulin was almost absent in normal mucosa, but was present in CRC cells (median 1.6 in normal epithelium vs. 12.0 in CRC, $p = 0.000$). Elevated normalized value of betaI-tubulin in CRC more then 12.7 and 9.7 was associated with lower disease-free ($p = 0.002$) and cancer-specific survival ($p = 0.022$) respectively. Moreover, increased level of betaIII-isotype in tumor budding was associated with lower disease-free survival in patients on 5-FU chemotherapy ($p = 0.010$).

**Conclusion:** These results demonstrate for the first time that betaI–tubulin expression is increased in CRC, but lower levels of this isotype are associated with worse survival. Expression of betaIII–tubulin is also increased in CRC, but higher levels of this molecule are associated with worse survival. Moreover, upregulation of betaIII–tubulin in the tumor budding in the invasive front could be important for determination of 5-FU resistant patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1472 COMPREHENSIVE METHYLATION ANALYSIS OF IMPRINTING-ASSOCIATED DIFFERENTIALLY METHYLATED REGIONS IN COLORECTAL CANCER

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**Introduction:** The expression of imprinted genes depends on the methylation status of differentially methylated regions (DMRs). The disruption of imprinting causes various congenital malformation syndromes, such as imprinting disorders, and is deeply involved in the development and progression of cancer. In colorectal cancer (CRC), aberrant methylation of DMRs within the IGF2/H19 imprinting domain has been reported. However, there have been no comprehensive analyses of methylation of DMRs in CRC.

**Aims & Methods:** We analyzed the methylation status of 38 DMRs in 106 CRC tissues and corresponding normal tissues. Cases with metastasis, preoperative chemotherapy, and inflammatory bowel diseases were not subjected to this study. We also investigated CpG island methylator phenotype (CIMP) using classical CIMP markers (hMLH1, MINT1, MINT2, MINT31, p16), and methylation status of long interspersed nucleotide element 1 (LINE1). These methylation statuses were quantitatively analyzed with bisulfite-pyrosequencing. Then we performed statistical analyses to clarify the relationships between the epigenetic conditions and clinicopathological factors of CRC.

**Results:** Among four DMRs in the IGF2/H19 domain, H19-DMR plays an important role for the expression of the imprinted genes, IGF2 and H19. We found that 44% of the cases showed hypomethylation at IGF2-DMR2 and 66% at IGF2-DMR0, whereas only 2% of the cases showed hypermethylation of H19-DMR and H19-promoter. The result indicated that hypomethylation of IGF2-DMRs was more frequent in IGF2/H19 imprinting domain in CRC. The comprehensive methylation analysis of 38 imprinted DMRs revealed that on average, $9.2 \pm 6.1$ DMRs per case were hypermethylated and $2.9 \pm 2.3$ DMRs were hypomethylated, indicating a frequent occurrence of hypermethylation. We found 6 particular DMRs to be aberrantly methylated in 50% or more of the CRC samples, i.e. high frequency aberrantly methylated DMRs (HF-DMRs). Of these, five DMRs (PEG1, TRAPPC9, NDN, NESP55, GNASXL) showed hypermethylation and the IGF2-DMR0 showed hypomethylation. Additionally, nine DMRs were aberrantly methylated in less than 10% of cases, i.e. DMRs resistant to aberrant methylation (RE-DMRs). Statistical analyses did not show any relationships between the aberrant methylation of imprinted DMRs and clinicopathological factors. We identified that 25% of cases showed a positive status of CIMP. However, there was no association between CIMP status and aberrant methylation of imprinted DMRs, including the hypermethylation of HF-DMRs and the hypomethylation of IGF2-DMR0. As for methylation status of LINE1, hypomethylation of LINE1 was associated with aberrant methylation of imprinted DMRs.

**Conclusion:** Our results revealed that in CRC, imprinted DMRs are likely to be hypermethylated. In the IGF2/H19 domain, however, IGF2-DMR0/2 hypomethylation is more frequent than H19DMR hypermethylation. We found that certain DMRs are susceptible to aberrant methylation, while another subset is resistant. Aberrant methylation of imprinted DMRs was not associated with clinicopathological factors. No association between hypermethylation of imprinted DMRs and CIMP positive suggested different causal mechanisms. However, global hypomethylation was associated with aberrant methylation of imprinted DMRs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1473 IS THE ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND COLORECTAL ADENOMA MEDIATED BY MUSCLE-DERIVED MYOKINES?

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**Introduction:** Exercise reduces the risk of colorectal cancer and adenoma but the mechanisms are not known. Exercise-induced muscle contraction releases multiple muscle-derived proteins (myokines) that exert effects on peripheral organs. These may mediate the beneficial effects of exercise including cancer prevention. Irisin is a myokine that increases thermogenesis and energy expenditure[1]. It is implicated in metabolic conditions (eg, diabetes mellitus) and has been shown to induce apoptosis in breast cancer cell lines but to date, has not been studied in colorectal cancer or adenoma.

**Aims & Methods:** We seek to determine whether the association between physical activity and colorectal adenoma is related to serum irisin levels. A case-control study was performed. Eligible subjects, aged 45–70 years, scheduled for ambulatory colonoscopy, were prospectively recruited. Baseline assessment was performed. Self-reported physical activity data was collected using the validated IPAQ Long questionnaire. Physical activity levels were characterized both as continuous and categorical variables. Venous specimens were drawn before colonoscopy.

All colonoscopies were performed by gastroenterologists from a single tertiary hospital. All polyp histology was reported by a pathologist blinded to anthropometric and physical activity data. Any uncertainty was reconciled by a second GI pathologist.

Consecutive cases with adenoma and matched controls with normal colonoscopy underwent body composition analysis by dual energy X-ray absorptiometry (DEXA). Skeletal muscle mass was quantified by skeletal muscle mass index, SMI ($kg/m^2$). Irisin levels (Biovendor Human Irisin Elisa Kit) were assayed. Logistic regression was used to evaluate associations.

**Results:**

| Variable (data presented as proportion or median and IQR) | Controls | Cases |
|---|---|---|
| Age (years) | 58(10) | 60.5(9) |
| Male gender, n (%) | 24(60) | 16(61.5) |
| Chinese race, n (%) | 39 (97.5) | 26(100) |
| Obese, n (%) | 4 (10) | 7 (26.9) |
| Charlson comorbid index category 0, n (%) | 35(87.5) | 23 (88.5) |
| Current smoker, n (%) | 2 (5) | 6 (23.1) |
| High physical activity, n (%) | 22(55) | 11(42.3) |
| Total body percentage fat | 32.1 (11.2) | 32.7 (9.4) |
| Skeletal muscle mass index ($kg/m^2$) | 6.2(2.1) | 6.5 (0.9) |
| Serum Irisin (ug/ml) | 2.8 (1.3) | 2.1 (2.4) |

66 patients were studied (see Table above). Irisin levels were significantly associated with the presence of adenoma (Odds ratio 0.61 [0.38–0.98], $p = 0.040$) even after adjusting for known confounders.

**Conclusion:** Higher irisin levels are associated with a lower likelihood of colorectal adenoma even after correcting for confounders including physical activity and direct measures of adiposity and muscle mass. This is in keeping with a protective role for irisin. This relationship should be explored in colorectal cancer patients and mechanistic insight should be sought.

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All other authors have declared no conflicts of interest.

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## P1474 COMPARATIVE MIRNA PROFILING IN PARALLEL COLORECTAL BIOPSY AND PLASMA SPECIMENS

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**Introduction:** MicroRNA has been found to play critical role in colorectal adenoma-carcinoma sequence. Recently, miRNA specific high throughput arrays became available to detect promising microRNA expression alterations even in colorectal cancer (CRC). While miRNA expression markers are well characterized in tissue, less is known about miRNA expression profiles in plasma samples.
**Aims & Methods:** The purpose of this study was to identify miRNA expression patterns between normal colonic (N), tubular adenoma (ADT), tubulovillous adenoma (ADTV) and colorectal cancer (CRC) plasma samples.Furthermore, our aim was to analyze the expression level of miRNA in matched tissue samples. Sixteen peripheral plasma samples and matched tissue biopsy samples (normal [N] n = 4tubular adenoma [ADT]n = 4; tubulovillous adenoma [ADTV] n = 4;colorectal cancer [CRC]n = 4) were also selectedand total RNA included miRNA was isolated.Matched MiRNA microarray experiments were conducted by GeneChip® miRNA 3.0 Array (Affymetrix). RT-qPCR (microRNA Ready-to-use PCR Human Panel I + II; Exiqon) was used for validation.
**Results:** Out of the 1733, the detectable number of miRNA, which could be found in each group was; N = 306, AD = 334, CRC = 321. Four miRNA (miR-4315, -519 e, -4257, -4253) showed altered expression between normal CRC groups in plasma. Expression of miR-4257 and miR-4253 are downregulated in CRC tissue samples moreover concentration of these miRNAs show upregulation in CRC compared to normal plasma pairs. MiR-4315 and miR-519 e are downregulated in both sample types in case of CRC, though higher expression was observed in normal plasma pairs. MiR-1972 was also selected and upregulation (FC = 0.5) in CRC was confirmed by RT-PCR in plasma furthermore positive correlation was observed in tissue. MiR-2116 and miR-548 p were upregulated only in tubulovillous adenoma compared to normal and tubular adenoma in plasma in contrast to tissue with a low concentration. Four miRNA were upregulated, three miRNA were downregulated in neoplastic lesions compared to normal in plasma, downregulated candidates showed upregulation in tissue pairs.
**Conclusion:** miRNAs were also found in peripheral blood system in a lower concentration compared to tissues. Systematic changes could observed in different stages. Circulating miRNAs of plasma could have a clinical significance in detection of neoplastic alterations.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1475 A SEVEN-GENE SIGNATURE PREDICTS OVERALL SURVIVAL OF PATIENTS WITH COLORECTAL CANCER

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**Introduction:** Colorectal cancer (CRC) is a major cause of global cancer mortality. Gene expression profiles can help predict prognosis of colorectal cancer, although with no firm conclusions. For most of studies, disease recurrence was used as the survival endpoint for analysis. In this paper, we aim to build a robust genes signature for prediction of overall survival (OS) in patients with CRC.
**Aims & Methods:** Fresh frozen CRC tissues from 67 patients were analyzed using Affymetrix HG-U133plus 2.0 gene arrays. Univariate survival analysis was used to screen genes associated with the overall survival of patients. A likelihood-based survival modelling approach was further adopted to unearth the optimal genes signature. The survival risk score system was built by BRB-ArrayTools, and validated in two external data sets of different platforms using receiver operating characteristic (ROC) curves.
**Results:** By performing univariate survival analysis, 6487 genes were found to be associated with the overall survival in patients with CRC from our cohort. KEGG analysis revealed that these genes were mainly involved in pathways such as endocytosis, axon guidance, spliceosome, Wnt signalling and ubiquitin mediated proteolysis. A linear prognostic model of seven-gene signature (NHLRC3, ZDHHC21, PRR14L, CCBL1, PTPRB, PNPO, and PPIP5K2) was constructed and weighted by regression coefficient, which divided patients into high- and low-risk groups. The OS for patients of high-risk group was significantly poorer compared with patients of low-risk group (hazard ratio [HR] = 25.79, $P < 0.001$). Interestingly, all seven genes were found to be significantly altered in CRC tissues as compared with adjacent normal tissues, indicating their potential role in CRC development. Importantly, this seven-gene signature was further validated as an independent prognostic marker for OS prediction in patients with CRC in other two cohorts (n = 55 for cohort I, area under the respective ROC Curves (AUC) = 0.715, P = 0.011; n = 272 for cohort II, AUC = 0.599, P = 0.027).
**Conclusion:** We developed a robust seven-gene signature that can predict the overall survival of patients with CRC, independently of the pathological staging. The gene signature may have important implications in clinical practice, especially for identifying CRC patients who are at high risk of mortality.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1476 FOUR ROUNDS OF TWO-SAMPLE FECAL IMMUNOCHEMICAL OCCULT BLOOD TEST SCREENING FOR COLORECTAL CANCER

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**Introduction:** Screening for colorectal cancer (CRC) using fecal immunochemical testing (FIT) requires successive rounds. Using two FITs (2-FIT) per screening round increases sensitivity and could maximize the yield of screening. However, limited data exists on 2-FIT screening over multiple rounds and the number of interval CRC (iCRC) found.
**Aims & Methods:** In this study we assessed the participation rate, diagnostic yield and iCRC of 2-FIT screening over 4 biennial successive rounds. From 2008 to 2015 average-risk subjects aged 50–74 years were invited for 4 rounds (R1-R4) of biennial 2-FIT screening. Per round, participants received two identical quantitative FITs (OC Sensor Micro, Eiken Japan) to sample from two consecutive bowel movements. FIT was considered positive if the hemoglobin (Hb) concentration was ≥10 μg Hb/g feces in at least one FIT. For each round, we excluded individuals with a history of CRC or IBD, colon imaging ≤2 years, a life expectancy <5 years, as well as those who died, moved away or had a positive FIT in previous rounds. Participation rate, positivity rate (PR), diagnostic yield, detection rate (DR) and positive predictive value (PPV) for advanced neoplasia (AN) and CRC were calculated. Diagnostic yield was defined as screenees with AN relative to all invitees. DR was defined as all screenees with AN or CRC relative to all participants. AN compromised CRC and advanced adenoma (>10 mm, or >25% villous component and/or high-grade dysplasia). iCRCs were identified through record linkage with the Dutch Comprehensive Cancer Centre.
**Results:** In total 3,131 were eligible at least once during the four screening rounds. Out of these, 1,882 (60%) were eligible to be invited in R4 (mean age 66 ± 5.3 years; 48% males). In R4, 64% (95%CI 61–66) participated (Table 1), 5.3% participated for the first time (62/1.172). The PR was 10.8% which was not significantly different from PR in R3 (p = 0.367). Although the numbers were too small to reach statistical significance, noteworthy is the increase in DR and PPV in R4 compared to R3 (p = 0.201, p = 0.175 respectively) (Table 1). In total, 72% (2.269/3.131) of all eligible subjects participated at least once. Of those attending at least once, cumulative PR was 28% (638/2.269, 95%CI; 26–30), cumulative DR of AN was 6.3% (144/2.269). After 4 rounds cumulative yield was 4.6% (144/3.131, 95%CI; 4–5) for AN and 0.8% (25/3131) for CRC. Two CRCs were detected in the fourth round, both pT1N0. In total, 25 screen detected CRCs, and only two iCRCs <2 years after a negative FIT were found.

**Table 1:** Overview results two-sample FIT screening in multiple rounds

| Round | Eligible invitees | Participation | Positivity rate | Detection rate AN | PPV AN CRC | |
|---|---|---|---|---|---|---|
| | N | N (%) | N (%) | N (%) | N (%) | % (95% CI) |
| **1** | 3057 | 1875 (61.3) | 239 (12.8) | 77 (4.1) | 13 (0.7) | 34% (28 – 41) |
| **2** | 2579 | 1582 (61.3) | 132 (8.3) | 27 (1.7) | 4 (0.3) | 21% (15 – 29) |
| **3** | 2287 | 1473 (64.4) | 141 (9.6) | 18 (1.2) | 6 (0.4) | 13% (8 – 20) |
| **4** | 1846 | 1172 (63.5) | 126 (10.8) | 22 (1.9) | 2 (0.2) | 20% (13 – 28) |
| | | P = 0.056 | P < 0.001 | P < 0.001 | P = 0.109 | P < 0.001 |

AN; advanced neoplasia, CRC; colorectal cancer, PPV; positive predictive value, CI; Confidence Interval.
**Conclusion:** Participation in 2-FIT screening is high and stable over at least 4 screening rounds. Detection rate and PPV dropped significantly over multiple rounds yet seem to increase in R4. Future research comparing these results with four rounds of 1-sample FIT screening is needed to confirm usability of 2-FIT screening and to evaluate if in a 2-FIT screening program decreases the incidence of interval cancers.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1477 ROLE OF FAECAL BIOMARKERS IN DETECTING COLORECTAL CANCER AND ADENOMA IN SYMPTOMATIC PATIENTS

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**Introduction:** Colorectal cancer (CRC) is the third most common malignancy in the world. The diagnosis can be difficult as symptoms of CRC are variable and have poor specificity. Most patients with symptoms have benign pathology but in an effort not to miss CRC, almost all patients undergo invasive colonic investigations. In the UK, the prevalence of CRC in this patient group ranges from 6–8%. Thus there is a quest for simple, non-invasive testing that can help streamline those with significant colonic pathology.
Guaiac faecal occult blood test (gFOBT), which is currently utilised in the bowel cancer screening programme, has relatively poor specificity for colorectal cancer and will be replaced with immuno-chemical testing (FIT) which has improved sensitivity and specificity. Conversely faecal calprotectin (FC) has good evidence for detecting inflammatory bowel disease (IBD) but its value in colorectal cancer is less well studied.
**Aims & Methods:** To prospectively analyse the role of faecal biomarkers (FIT and FC) to detect colorectal cancer and adenomas in patients presenting with lower gastrointestinal (GI) symptoms. 799 consecutive patients (median age 67 (29–93) years; 50.7% women) with lower GI symptoms referred for investigations from the primary care (as per national referral pathway) were recruited prospectively from colorectal and gastrointestinal clinics. After applying a strict exclusion criteria, 434 patients were included who had complete colonic investigations. FIT and FC were measured in all patients and final outcomes recorded. All analysis was carried out using Matlab R2011b. Groups were compared using the Mann-Whitney U test. Results were considered significant if $p < 0.05$.
**Results:** FIT returned a sensitivity of 92% and specificity of 87% for detection of colorectal cancer; AUC of 0.96 (CI 0.90–1.00). FC had sensitivity of 68% and specificity of 84% for detecting colorectal cancer; AUC of 0.83 (CI 0.73–0.93). The combination of both FIT and FC had minimal improvement over FIT alone; sensitivity 92% although specificity improved to 94% with AUC of 0.96 (CI 0.90–1.00). For adenoma detection, FIT was superior with a sensitivity of 69.0% and specificity of 70.3%; AUC 0.71 (CI 0.63–0.79) with FCP showing no benefit compared to not testing. For detection of both cancer and adenomas, FIT again was superior with a sensitivity of 76% and specificity of 70%; AUC of 0.77 (CI 0.71–0.83) and FCP showing no benefit compared to not testing.
**Conclusion:** FIT is a good biomarker for detection of colorectal cancer in symptomatic patients. The combination of both FIT and FC improves specificity but not sensitivity.
**Disclosure of Interest:** R. Arasaradnam: R Arasaradnam has provided educational lectures on behalf of ThermoFisher ltd. Which provide FC analysis
All other authors have declared no conflicts of interest.

## P1478 MORPHOLOGICAL ANALYSIS OF CARCINOMAS IN JAPANESE PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

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**Introduction:** It is generally accepted that carcinomas arising from adenomas in familial adenomatous polyposis (FAP) patients. On the other hand, a few cases of carcinoma with depressed type without adenoma has been reported. The closer examination of morphology of carcinomas in FAP patients has not been reported.
**Aims & Methods:** [Aim] To clarify the morphology of carcinomas in FAP patients.
[Material and Method] From 2000 to 2012, 170 patients of FAP with carcinomas were operated in 23 institutes participated in Study Group for FAP in JSCCR. In the study, 373 lesions of carcinoma were investigated. To clarify the morphology according to the development of carcinomas, 238 lesions of superficial type of carcinoma were evaluated in comparison with the data of 4019 lesions of early colorectal carcinoma* as non FAP Japanese patients.
**Results:** In 170 patients, 238 lesions were superficial type of carcinoma and 135 lesions were advanced carcinoma (type1 :19, type2 :100, type3 :10, type4 :0, type5 :6). In 238 lesions of superficial type of carcinoma, 10 lesions of depressed type were diagnosed (4.20%) in 9 patients. The other 228 lesions were categorized as protruded type or flat type (95.8%). As a localization, depressed type of carcinoma were 6.49% (5/77) in the right side colon. 2.56% (3/117) in the left side colon, 4.55% (2/44) in the rectum. In FAP patients, the lesion of depressed type of carcinoma was significantly less than non FAP patients (4.20%, 10/238 vs 16.7%, 670/4019, $p < 0.001$).
**Conclusion:** In FAP patients, carcinoma was widely accepted arising in the numerous adenomas as polyps. A few cases of depressed type of carcinoma in FAP patients were reported. But the frequency was unclear. This study reported the analysis of morphology of carcinomas in FAP patients compare with non FAP patients. Depressed type of carcinoma were present and diagnosed in plural institutes. In FAP patients, depressed type of carcinoma is present but less than non FAP patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1479 FEATURE- EXTRACTION FROM HISTOLOGY USED IN A COMPUTER-AIDED GRADING SYSTEM FOR COLON CANCERS

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**Introduction:** Colorectal cancer (CRC) currently ranks as one of the most common cancers worldwide, being the fourth leading cause of cancer death. Accurate diagnosis and staging requires histology and determines therapeutic approach.
**Aims & Methods:** Our aim was to investigate colorectal cancer histologically and immunohistochemically, identifying and quantifying morphometric elements through fractal analysis and using an automatic system based on artificial intelligence for diagnosis and classification. We have obtained ethical clearance from the local committee and all included patients provided informed consent for participating in our study. We have prospectively selected patients between September 2014 and October 2015 that underwent surgery for previously diagnosed CRCs. Biopsy material was obtained for diagnostic through biopsy during colonoscopy or postoperatively after surgery with curative intention. Patients were followed post-intervention and the tissue was processed by techniques of classic histology (hematoxylin-eosin staining and trichromic staining with green light by Goldner-Szeckelly method) and immunohistochemistry (anti-p53, anti-Ki67, PCNA and Anti-VEGF-C). We observed histological and immunohistochemical changes, subjecting a median of 50 images per patient to computer analysis with an in-house tool for obtaining fractal dimension, as well as ImageJ for GLCM (histogram of co-occurring greyscale values). Neural networks were applied for diagnosing and classification of tumor types, as well as for staging. We calculated the sensitivity, specificity, positive and predictive predictive values of the system.
**Results:** We included in the study 96 consecutive patients (58 men) - 38 sigmoid tumors, 27 tumors of the descending colon, 12 tumors of the transverse colon, 10 on the ascending colon and 9 of the caecum. Fractal analysis of the nuclear chromatin layout identified major differences between well differentiated tumors compared to other tumor types. We also found significant differences between adenocarcinomas and other histological types; however, we have not encountered significant differences between colloid tumors and signet ring cell tumors. Fractal analysis of immunohistochemical images showed significant differences ($p < 0.0001$) between the anti-Ki67, anti-p53, anti-VEGF and PCNA and normal mucosa; the analysis also showed significant differences between early stages (good and very well differentiated) and advanced ones. Artificial intelligence could distinguish tumor tissue from normal mucosa in 98.7% of cases, classifying tumors with an accuracy of 87.2%, sensitivity

88.4%, specificity 83.2%, positive predictive value 83.11% and negative predictive value of 86.8%.
**Conclusion:** Computerized processing and feature extraction from histological and immunolabeled images can provide additional data for diagnosis, classification and staging of malignant tumors of the large intestine. Neural networks are a suitable tool for automatic interpretation of these data, which may serve as a diagnostic and decision support for colorectal cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1480 ADENOMA DETECTION WITH ENDOCUFF-ASSISTED COLONOSCOPY

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**Introduction:** Colonoscopy is considered the gold standard method for detecting colonic neoplasia worldwide. However, polyps are still missed substantially in screening colonoscopy, especially those less than 10 mm in size, which are located in the sigmoid and flexures, as well as behind multiple folds and haustrae. Several techniques, such as cap-assisted colonoscopy (CAC), were developed to improve the rate of polyp detection, and some studies reported that CAC promoted polyp detection. A new device, Endocuff (EC), was also developed with the hope of improving the adenoma detection rate (ADR). Recently, several studies have shown that EC-assisted colonoscopies (EACs) improved polyp detection rate compared to standard colonoscopies. The aim of this study was to compare the ADR of EAC with that of CAC in screening.
**Aims & Methods:** Among all the patients who underwent screening colonoscopy at the Akashi Medical Center, Hyogo, Japan, over a period of 3 months between January to May 2016, those who passed the exclusion criteria (those with partial colonic resection, known colonic obstruction, colonic adenoma or cancer, suspected or proven lower GI bleeding, and inflammatory bowel disease) and provided informed consent were randomly assigned to the EAC or CAC group. All examinations were performed by three endoscopists. Prospectively, we could collect data on cecal and ileal intubation rates, insertion time, withdrawal time, colon cleanliness, ADR, clinicopathological characteristics of polyps, and complications. Cecal intubation was confirmed by the documentation of the appendiceal orifice or cecal valve. Withdrawal time was measured from the cecum to the anus, without counting the time spent on suctioning of fluid or polypectomy. We also assessed the difference in polyps according to size, location, and morphology by using EAC and CAC. The data were statistically analyzed.
**Results:** A total of 159 patients were enrolled in this study; EAC and CAC were performed on 84 and 75 patients, respectively. Patient characteristics and colon cleanliness were not significantly difference between the groups. The cecal intubation rate was comparable between the two group (98% vs. 99%, $p = 0.63$).The insertion and withdrawal times were also not significantly different ($8.25 \pm 5.98$ min, $7.95 \pm 1.44$ min with EAC vs $7.91 \pm 5.51$ min, $8.35 \pm 1.98$ mm with CAC; $p = 0.71$ and 0.14, respectively). On the other hand, the ileal intubation rate was significantly lower in EAC than in CAC (35% vs. 83%, $p < 0.01$). A total of 162 adenomas were detected in this study. The ADR in EAC was not significantly different compared with that in CAC (53% vs. 59%, $p = 0.43$). EAC also detected a similar number of adenomas per patient compared to CAC (1.03 vs. 1.00, $p = 0.88$). The location of adenomas was also did not differ between the groups (cecum, 3(3%)/5(7%); ascending colon, 19(22%)/14(19%); transverse colon, 16(18%)/19(25%); descending colon, 9(10%)/5(7%); sigmoid colon, 32(37%)/25(33%); and rectum, 8(9%)/7(9%) in EAC/CAC, respectively). The number of adenomas according to size and morphology of the polyps also did not differ significantly between the groups ($p = 0.64$). Minimal mucosal lacerations were observed in 17 patients (EAC: 16 vs. CAC: 1; $p < 0.01$). Major complications were not observed.
**Conclusion:** This study showed similar maneuverability and ability of polyp detection with EAC and CAC. However, the ADR (53% and 59%) in both groups was higher compared with that of standard colonoscopy, which has been reported. One of the possible reasons for the similarity in ADR between the groups was considered to be the same type of equipment used to flatten large mucosal folds during withdrawal of the instrument. Cecal intubation rate was similar in the two groups, but the ileal intubation rate was significantly lower in EAC than in CAC. However this result will not affect the clinical outcome of ADR because lesions that extend into the cecal valve are very rare. In conclusion, EAC was as safe and efficacious as CAC in screening.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1481 CLINICOPATHOLOGICAL, MOLECULAR AND ONCOLOGICAL FEATURES OF SPORADIC EARLY ONSET COLORECTAL CANCERS

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**Introduction:** Approximately, 15% of colorectal cancers occur before the age of 50, mostly related to inflammatory bowel diseases, Lynch syndrome (LS), and polyposis syndromes. However, up to 7% of colorectal cancers occur in patients with less than 50 years of age (Early Onset Colorectal cancers - EOCRC) with no evidence of familial predisposition or belonging to hereditary syndromes.
**Aims & Methods:** AIM: To study a large population of EOCRC with no predisposing genetic risk factors in order to define the clinicopathological features and the stage at presentation. We also aimed to evaluate the correlation between histological and molecular patterns, clinicopathological features and oncological outcomes. METHODS: All cases of EOCRC were identified between 2006 and 2014 from a the prospectively maintained databases of the two oncological surgeries. Patients who had LS, inflammatory bowel disease, polyposis syndrome, or a known family history for these conditions were excluded. Medical records from all included patients were reviewed and data was extracted on patient demographics, clinical features, oncological treatment and postoperative follow-up. Tumours histological features and molecular data, including KRAS genotype, MLH1 and MSH2 protein levels, as well as Ki-67, p53 and thymidylate synthase (TS) protein levels were also collected.
**Results:** Ninety-four cases (54% males) were identified. The mean age at surgery was 43 years. The most common site of primary tumour was the rectum (40%), followed by left colon (32%) and right colon (27%). 83% of patients were symptomatic at the time of diagnosis: the most common presenting symptoms were abdominal pain, haematochezia, rectal bleeding. Half of EOCRCs showed an advanced stage with either stage III (34%) or stage IV (16%) at presentation. Histologically, 10% of the cancers were well differentiated, 70% were moderately differentiated, and 20% were poorly differentiated. Mucinous and signet-ring cell histology was seen in 20 (21%) and 2 (2%) cases, respectively. Seventeen patients (22%) had a first- or second-degree relative with CRC outside of a defined syndrome (FAP or HNPCC), and 43% with any type of cancer, regardless of location. Smoking rate in the EOCRC group was 36%, whereas 21% of patients consumed alcohol daily. The majority of patients showed a normal weight, with a mean BMI of 23.4. Regarding the molecular features, 7.2% and 0% lacked of MLH1 and MSH2 expression, respectively, and37% harbored KRAS mutation; 36% and 21% revealed low p53 and high TS levels, respectively. The median follow-up after surgery was 35 months. The overall the 1-year survival was 91%, while at 5 years it dropped to 57%.
**Conclusion:** EOCRCs appear frequently as aggressive cancers located in the sigmoid colon and rectum, are DNA mismatch repair proficient and most patients are symptomatic at the time of presentation. Since screening programs do not include patients under 50 years of age, overall prognosis of EOCRCs is poor related to the advanced stage of disease at the time of diagnosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1482 THE IMPACT OF PATIENT EDUCATION WITH SMARTPHONE APPLICATION ON THE QUALITY OF BOWEL PREPARATION FOR SCREENING COLONOSCOPY

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**Introduction:** Colorectal cancer is the 3rd most commonly diagnosed cancer in South Korea. The standard method for evaluating the colon is the colonoscopy procedure. Proper bowel preparation is essential for successful examination. A sub-optimal bowel preparation can lead to compromised exams with missed polyps, an increase in procedure time, and aborted exams. Few studies have evaluated the use of smartphone applications as a means of educating and improving the quality of bowel preparation. Therefore, we created a smartphone

application for patients to use as a preparation guide before undergoing a colonoscopy.
**Aims & Methods:** A total of 142 patients (M:F = 84:58, mean age 43.5 ± 9.3 years-old) who were scheduled to undergo a screening colonoscopy in a health examination center were enrolled in this study. The study was conducted as a prospective endoscopist-blinded, controlled design. Participants were divided into two groups, one group was asked to use a new smartphone application that we had newly developed that educates the user on colonoscopy preparation (Smart group, N = 71), the other group received the existing verbal and written instructions (Control group, N = 71).
**Results:** The quality of bowel preparation, assessed using The Boston Bowel Preparation Scale (BBPS) was significantly higher in the smart group than control group (7.70 ± 1.1 vs. 7.24 ± 0.8; p = 0.007 by t-test). Although no significant differences were found between the two groups in cecal insertion time, withdrawal time was significantly higher in the smart group than control group. In addition, the number of patients with polyps between two groups has no significant difference (23/71in smart group vs. 15/71 in control; p = 0.129).
**Conclusion:** Our study is showing that the bowel preparation by smartphone application was significantly better bowel preparation quality as assessed by the BBPS. Smartphone application might replace the written paper instruction, soon. More studies are needed to show the exact impact of bowel preparation with smartphone application.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1483 THE PREDICTIVE VALUE OF FERRITIN IN OLDER PATIENTS IN THE DIAGNOSIS OF COLON CANCER


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**Introduction:** Ferritin is an indicator of iron deficiency. However, it may produce false results in the presence of acute/chronic inflammation. In older patients, colon cancer is an important cause of morbidity and mortality.
**Aims & Methods:** The aim of this study was to determine the predictive value of ferritin and ferritin-transferrin saturation combination for predicting the presence of colon cancer in older patients. 600 patients aged >65 year-old were included into the study. Along with gastroscopic and colonoscopic findings, serum iron profile and C-reactive protein were also recorded. Patients were stratified into three groups according to their iron profiles: group 1: ferritin < 50 μg/L; group 2, Ferritin < 100 μg/L; group 3, Ferritin < 50 μg/L were the indicators for iron deficiency. If ferritin value was higher than 50 μg/L and transferrin saturation is below 16%, iron deficiency diagnosis was made.
**Results:** 528 patients had no upper and lower endoscopic findings that can result iron deficiency and 72 patients had colon cancer with normal gastroscopic findings. C-reactive protein values were found to be significantly high in the colon cancer group (p < 0.001). Ferritin value was found to be similar in the colon cancer and normal colonoscopy groups. In the colon cancer group, by means of showing the presence of iron deficiency; group 1 had 63% sensitivity and 53% specifity, group 2 had 79% sensitivity and 20% specifity, group 3 had 91% sensitivity and 49% specifity. In the ROC analysis, the AUROC value was found to be 0.704 for group 3. The patients in group 3 had significantly higher C-reactive protein values than the ones in group 1 and 3.
**Conclusion:** In older patients, normal ferritin values is not enough to disregard iron deficiency diagnosis. In this situation by using the transferin saturation, a possible presence of iron deficiency should be investigated. Patients with transferin saturation lower than 16% should undergo endoscopic examination with the diagnosis of iron deficiency.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1484 COLORECTAL CANCER SCREENING FROM THE VIEWPOINT OF ITS TARGET POPULATION – RESULTS OF SURVEY


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**Introduction:** Result of colorectal cancer (CRC) screening programs are often presented from the viewpoint of stakeholders, care providers and endoscopists. Studies describing the viewpoint of clients – the target population are rare. Interview/questionaire with direct care provider (general practitioner, endoscopist) may be skewed. Level of participation in CRC screening program in the Czech Republic is about 30%.
**Aims & Methods:** This study aims to acquire independent opinion from the viewpoint of CRC screening target population regarding the CRC screening information sources, reasons for and against participation in the screening. We want to discover the troublesome points in the screening from the practical view of the clients.
Anonymous questionnaires were distributed to relatives of pre-gradual university students, to students of The University of the Third Age Masaryk University Brno (aged over 50) and to patients of gastroenterology department I two periods in years 2013 and 2015. Following issues were found out: demography and CRC in family, sources of CRC program information, reasons for non-participation in the screening, practical troubles with screening tests realization and circumstances that can stimulate the participation.
**Results:** Completed questionnaire was acquired from 404 persons:34% male (139), average age 65.0 ± 8.2 years. We got information from 116 relatives of students (response rate 31%), 215 adult students and 73 patients coming for screening colonoscopy (both with response rate over 90%). CRC in family history was recorded in 15.6% of respondents. Only 17 persons (4.2%) never heard about CRC screening. General practitioner was the main information source of screening (up to 75%), following classical media: TV, radio – 35%, friend or family member advice – 25%, internet – 14%, personalized invitation – 13% and from publicity stunt– 4%. More than 16% of responders did not participate in the screening, their main reasons were: lack of time– 40%, lack of interest in preventive examination 25%, fear of endoscopy– 35% and fear of positive result– 30%. Majority of respondents (78%) had personal experience with FOBT, (in 27% followed by colonoscopy) and they reported inhibitions to manipulate with stool and inappropriate toilet bowl for stool collection as main troubles. Fear of colonoscopy and fear of bowel preparation was reported in 70% (35%). Fear of cancer on endoscopy was mentioned in 53%. According to respondents view, participation rate might improve due to better explanation of screening principles and due to arrangement of painless colonoscopy.
**Conclusion:** One half of clients experience the screening tests with no troubles. Fear of colonoscopy and fear of positive result on test were the main referred problems for participation in regular screening. One quarter of responders feel technical problems with stool catch. Support of CRC screening might be focused on decrease the fear of examination and tools for easy stool catch. Preference of primary colonoscopy with analgosedation could be useful.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1485 EARLY ONSET COLORECTAL CANCERS VS SPORADIC COLORECTAL CANCERS: A CLINICOPATHOLOGICAL AND MOLECULAR EVALUATION


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**Introduction:** Colorectal cancers (CRCs) developing before the age of 50, with no evidence of familial predisposition or belonging to hereditary syndromes are defined as Early Onset Colorectal cancers (EOCRCs). Case series of EOCRCs have been studied, however, little is known about their predisposing factors and the molecular pathways that promote the early onset of these tumours.
**Aims & Methods:** AIM: to evaluate if EOCRCs may be defined as a distinct entity by comparing their clinicopathological, histological and molecular features to a consecutive series of sporadic CRCs developed in patients over 50 years of age. METHODS: A series of 94 EOCRC identified from a prospectively maintained database of the two oncological surgeries was compared to a consecutive series of 192 sporadic CRCs from patients older than 50 years (from the same hospital) that had been analysed and reported in a previous study by our research group. Medical records from all included patients were reviewed and data was extracted on patients demographics, clinical features, and tumours histological and molecular data, including MLH1 and MSH2 protein levels, as well as p53 and Thymidylate synthase (TS) protein levels.

**Results:**

| | EOCRCs (n = 94) | Sporadic CRCs (n = 192) |
|---|---|---|
| Age, years (Average ± SD) | 43.2 ± 3.9 | 67.3 ± 12.1 |
| Sex Male Female | 51 (54%) 43 (46%) | 107 (56%) 85 (44%) |
| Location Right colon Left colon | 30 (32%) 64 (68%) | 83 (43%) 109 (57%) |
| TNM staging 0-II III-IV | 50% 50% | 47% 53% |
| Missmatch repair genes status<br>MLH1 deficiency<br>MSH2 deficiency | 7.2% 0% | 9.9% 4.7% |
| p53 levels (low) | 36% | 36% |
| Thymidylate synthase levels (high) | 21% | 21% |

The mean age at surgery of EOCRCs and controls was 43 and 67 years, respectively. Regarding cancer location, 57% of the control CRCs were located in the left colon, whereas the most common site of EOCRCs was the rectum (p = 0.16). Stage II lesions were the most frequent in the controls (47% of the cases - no stage 0 or stage I cancers were present in this group) whereas the advanced stages III and IV were present in 40% and 13% of the cases, respectively. Similarly, in the EOCRCs group stage III and IV lesions represented 50% of patients, although stage IV cancers seem to occur more often (16%). Histologically, EOCRCs showed a tendency of higher incidence of poorly differentiated tumours compared to control CRCs (20% vs. 15%) (p = 0.29). Mucinous histology and signet-ring cell tumours were present in 15% and 0% of controls compared to 21% and 2% in the EOCRC cohort. Regarding the molecular features, 7.2% and 0% in the EOCRC and 9.9% and 4.7% lacked MLH1 and MSH2 expression, respectively. In both groups, immunohistochemistry analysis showed similar low p53 levels in 36% of cases and high TS levels (21% in both groups).

**Conclusion:** The genetic basis in the majority of early onset colorectal carcinomas remains unknown, However, most EOCRCs appear to arise through the same pathways as sporadic CRCs, such as the classical adenoma-carcinoma sequence. EOCRCs appear more frequently as aggressive cancers, related to the advanced stage of disease and the delayed diagnosis since patients with less than 50 years of age are not included in screening programs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1486 SCREENING COLONOSCOPIES IN FIRST-DEGREE RELATIVES OF PATIENTS WITH COLORECTAL CANCER COMPARED TO AVERAGE RISK POPULATION


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**Introduction:** First-degree relatives (FDR) were considered to have higher risk of colorectal cancer compared with general population. Some recent studies showed that the risk of FDR is not as high as previously expected and curret guidelines (ESGE, European guidelines) doŕt recommend different surveillance for them. The aim of our study was to compare the detection of neoplastic lesions during screening colonoscopy in FDR and average risk population.

**Aims & Methods:** The data from all screening colonoscopies performed in one non-university gastroenterology center from january 2012 to december 2015 were recorded to database in MS Excel. The main parts of the database comprise of epidemiologic data about the patient including family history of colorectal cancer, data about examination, histologic results and complications. The results of colonoscopies in FDR and average risk patients were compared, the chi-square and Student t test were used to compare dichotomous and continous variables considering level od significance of .05.

**Results:** 1677 screening colonoscopies were performed in total, of them 191 in FDR and 1486 in average risk individuals. Because of nonhomogenous gender distribution in both groups (p = 0.007), men and women were compared separately. FDR in both groups were significantly younger. The number of examinations after positive FOBT and primary colonoscopies were not significantly different between the groups. The detection of neoplastic lesions represented by PDR, ADR, advanced ADR, number of carcinomas and APCR was not higher among FDR. See the table.

| | Men FDR (81) | Men (784) | p | Women FDR (110) | Women (702) | p |
|---|---|---|---|---|---|---|
| **Age** | **60.4** | **62.9** | **0.005** | **61.6** | **63.7** | **0.013** |
| FOBT/primary c. | 38/43 | 396/415 | 0.742 | 50/60 | 389/313 | 0.051 |
| PDR | 58 (71.6%) | 615 (78.4%) | 0.15 | 65 (59.1% | 414 (59.0% | 0324 |
| ADR | 42 (51.9%) | 451 (57.5%) | 0.326 | 44 (40.0%) | 259 (36.9%) | 0.531 |
| Advanced ADR | 16 (19.6%) | 167 (21.3%) | 0.745 | 11 (10.0%) | 80 (11.4%) | 0.666 |
| Carcinoma | 1 (1.2%) | 17 (2.2%) | 0.575 | 2 (1.8%) | 7 (1%) | 0.350 |
| APCR | 0.938 | 1.247 | 0.089 | 0.700 | 0.581 | 0.255 |

**Conclusion:** There were no differences in detection of neoplastic lesions between FDR and average risk population, but FDR were significantly younger at the time of screening colonoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1487 A PILOT STUDY TO ASSESS THE EFFICACY OF PROPHYLACTIC ADMINISTRATION OF ANTIBIOTIC FOR ENDOSCOPIC SUBMUCOSAL DISSECTION IN COLORECTUM


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**Introduction:** Endoscopic submucosal dissection (ESD) is accepted as one of the treatments for en bloc resection of large superficial colorectal lesions. However, the risk of perforation is high compared to conventional endoscopic mucosal resection (EMR)[1]. Peritonitis caused by the perforation in colorectum requires surgical treatments. Therefore, prophylactic administration of antibiotic in colorectal ESD is considered necessary for all cases, as it might avoid peritonitis from perforation, it is very difficult to predict about occurrence of delayed[2]. But some studies suggested few bacteremia and low risk on infectious complication after colorectal ESD[3,4].

**Aims & Methods:** The aim of our study is to assess the efficacy of prophylactic administration of antibiotics for endoscopic submucosal dissection in the colorectum. A total of 257 consecutive patients that were not administered with Prophylactic antibiotic treatment before and after ESD were enrolled in this study. Another 252 consecutive patients who have previously received colorectal ESDs with Prophylactic antibiotic treatment were included as a historical control. Treatment outcomes, body temperature, abdominal symptom and inflammatory reaction of the blood investigation (White blood cell [WBC] and °C reactive protein [CRP]) were compared between non-antibiotic and antibiotic groups. In the non-antibiotic group, we administered antibiotics to the particular cases in which temperature of the body was over 38.0°C and peritoneal irritation sign was encountered after ESD. Second generation of Cephalosporins were used for antibiotic group. All of ESD procedures were conducted under CO2 insufflation.

**Results:** Between non-antibiotic and antibiotic groups, there was no significant difference in the mean age (66.8 ± 10.9 vs. 67.8 ± 10.0), the mean tumor size (33.7 ± 20.4 mm vs. 35.2 ± 20.1 mm), ratio of muscular injury or perforation (13.2% vs. 10.7%), the mean amount of rise in temperature (0.41 ± 0.47°C vs. 0.42 ± 0.47°C) and CRP (0.43 ± 0.81 vs. 0.44 ± 0.82) on the next day of ESD procedure. The mean operation times, the number of twofold increase in WBC and abdominal tenderness were 77.2(± 57.6)/97.2(± 72.6) minutes, 6/17 cases and 9/17 cases, respectively ($P < 0.05$). Among the cases with muscular injury/perforation, there was no significant difference in all of the treatment outcome between non-antibiotic group and antibiotic group. Antibiotic treatments were required to 5 cases in non-antibiotic group because of physical symptoms (a high fever over 38°C and muscular defense) on the next day of ESD procedure associated with perforation. But no surgical treatment was needed. One delayed perforation occurred in non-antibiotic group, but it was treated only with a course of antibiotics. In summary, prophylactic administration of antibiotics wasn't necessary if adverse events didn't occur during and after ESD. Even if adverse event like perforation was encountered, it is enough to manage conservative treatment by administration of antibiotics after adverse event occurred.

**Conclusion:** There is no efficacy of prophylactic administration of antibiotics pre- and post-ESD in this study.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1488 THE OUTCOMES OF SELF-EXPANDING METAL STENTS AS A BRIDGE TO CURATIVE RESECTION IN PATIENTS WITH COLORECTAL CANCER PRESENTING WITH BOWEL OBSTRUCTION

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**Introduction:** Approximately 30% of colorectal cancers present with colonic obstruction. Self-expanding metal stents (SEMS) can be placed endoscopically as a bridge to surgery, allowing relief of the obstruction and time to improve the patient's physical condition prior to curative resection. A systematic review has suggested that this approach is associated with lower rates of stoma formation, shorter lengths of stay, lower complication rates and a higher rate of primary anastomosis when compared to surgery to relieve the episode of obstruction. However, there is a lack of randomised controlled trial data directly comparing the two approaches.

**Aims & Methods:** Hospital Episode Statistics (HES) is an administrative database of data on all elective and emergency care episodes in hospitals in England. Patients admitted with colonic obstruction due to colorectal cancer were identified in HES. Patients were subdivided into two cohorts: SEMS insertion prior to surgery and surgery only. Patients with metastatic disease at the time of presentation were excluded. Mortality, emergency readmission within 30 days, postoperative complications and patient demographic factors were examined using univariate and multivariate regression analysis. Propensity score matching was then used to compare outcomes between the SEMS and control cohorts.

**Results:** Between January 2006 and December 2015, 4,849 patients (mean age 71 (IQR 63–80) years and 51.9% male) who underwent surgery only and 409 patients who had a SEMS as a bridge to surgery (mean age 69.7 (IQR 62–79) years and 56.7% male) were identified. On univariate analysis, SEMS insertion became more common over the study period with only 2.7% of the total procedures being carried out in 2006 compared to 14.7% in 2013 ($p < 0.001$). Death within 30 days of resection was significantly lower in the SEMS cohort (2.0% vs. 9.7% respectively, $p < 0.001$), as was the risk of emergency readmission within 30 days (8.8% vs.15.0%, $p = 0.001$) and the rate of major complications (5.38% vs. 18.36%, $p < 0.001$). Those undergoing a SEMS insertion had lower rates of post-operative anastomotic complications (0.24% vs. 1.53%, $p = 0.035$), sepsis (1.71% vs. 5.74%, $p = 0.001$), thrombosis (0.24% vs. 2.03%, $p = 0.011$) and acute cardiovascular events (2.2% vs. 7.88%, $p < 0.001$) when compared to surgery alone.

Multivariate analysis revealed that those undergoing a SEMS were less likely to be female (OR 0.80 (95% CI 0.65–0.99), $p = 0.036$), live in the East (0.15 (0.07–0.32), $p < 0.001$) or West Midlands (0.20 (0.11–0.35), $p < 0.001$) and were less likely to have major comorbidities (Charlson score of 5 or more 0.60 (0.44–0.81), $p = 0.001$). Following propensity matching, there was a small but not significant difference in survival between the SEMS and control cohorts at 30 days (98.0% vs. 96.2% respectively, $p = 0.1426$) and at 12 months (89.3% vs. 86.5% respectively, $p = 0.2127$). However, patients undergoing a SEMS procedure prior to surgery continued to have a significantly lower rate of emergency readmission within 30 days of resection when compared to those undergoing surgery only (8.7% vs. 20.4% respectively, $p < 0.001$).

**Conclusion:** In this retrospective, matched cohort study of patients with obstructing colorectal cancer undergoing either surgery alone or a SEMS as a bridge to curative surgery, we have demonstrated a significantly lower risk of emergency readmission within 30 days in the SEMS cohort. Patients undergoing a SEMS also appear to have a much lower risk of post-operative complications.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1489 IDENTIFICATION OF THE IRINOTECAN TOXICITY RELATED VARIANTS BY WHOLE EXOME SEQUENCING ANALYSIS

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**Introduction:** Concurrent irinotecan and fluorinated-pyrimidine is a common first-line therapy for metastatic colorectal cancer (mCRC). Although prolonged survival is associated with regimens involving irinotecan, severe neutropenia occurs in 20–35% of mCRC cases treated with irinotecan regimens.

**Aims & Methods:** To predict the risk of irinotecan toxicity for individual patients precisely, it is important that determining new biomarkers in addition to known markers; *UGT1A1*28* and *UGT1A1*6* is important, because patients without *UGT1A1*28* or **6* do experience severe irinotecan toxicity. Therefore, we identified the genetic variants associated with the toxicity by whole exome analysis. A case-control study was performed with patients bearing no *UGT1A* variations (loci of *UGT1A1*6*, **27*, **28*, **60*, *UGT1A7* (387 T, 622 T), *UGT1A9*1b*) who exhibited hematologic toxicity in entire course of irinotecan therapy ($n = 5$) and patients bearing one of *UGT1A* variations and exhibited sever toxicity in the first course treatment ($n = 5$) as case group and patients with no *UGT1A* variations and no sever toxicity were used as control group ($n = 5$). Whole exome sequencing (WES) was performed with genomic DNAs extracted from white blood cells and next generation sequencer; NextSeq 500, and then mapping and variant calling were done by BWA and GATK software, respectively. The annotation of each variations were performed by SnpEff software with dbNSFP database to evaluate the impact of variations on protein level. Validation genotyping with specific hydrolysis probes and primers was done by real-time PCR ($n = 75$). The Cochran-Armitage trend test was used to examine the linearity of the relationship between genotypes and irinotecan toxicity.

**Results:** Among numerous variations obtained by WES, single nucleotide polymorphisms (SNPs) were ranked by standardized difference based on the frequencies of each allele between the case and control and the *P* value of the trend test. As a result, top 5 variations were further analyzed to validate. In 75 patients, linkage disequilibrium analysis showed no correlation between the 5 variations and *UGT1A* polymorphisms, and the Hardy-Weinberg equilibrium *P* value for each locus examined in this study was higher than 0.05. The linearity of the relationship with irinotecan toxicity were observed in the SNPs in *APCDD1L*, *R3HCC1*,*MKKS*, *EDEM3* ($P < 0.05$) and a SNP in *OR51I2* ($P = 0.052$) in a sub-population ($n = 68$) excluding known high risk patients with homozygous of the *UGT1A1*28*, **6*, and these compound heterozygous. Interestingly, the homozygous of *R3HCC1* variation showed no hematologic toxicity in both FOLFIRI and FOLFOX treatments ($N = 117$).

**Conclusion:** The irinotecan toxicity related genetic variants identified in this study would be useful for prediction of irinotecan toxicity in addition to *UGT1A1* polymorphisms.

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All other authors have declared no conflicts of interest.

## P1490 GOOD BOWEL PREPARATION INCREASED THE NUMBER OF ENDOSCOPICALLY DETECTED POLYPS WHICH WAS WELL CORRELATED WITH DETECTION OF ADVANCED NEOPLASIA

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**Introduction:** Detecting colorectal adenoma, especially advanced neoplasia (AN), is effective in reducing colorectal cancer incidence and mortality. Therefore, improving bowel cleanliness would be important to increase adenoma detection rates (ADR) or polyp detection rates (PDR). Recent studies, however, reported that PDR or ADR appeared to be slightly lower, rather than higher, for excellent preparations compared with good.

**Aims & Methods:** The aim of this study was to evaluate PDR, the number of endoscopically detected polyps and AN detection rate (ANDR) stratified by the Boston Bowel Preparation Scale (BBPS). This study was a retrospective single center cohort study of consecutive patients who underwent colonoscopy from January 2015 to November 2015 at Toyonaka Municipal Hospital. We evaluated the association between bowel preparation quality by using the BBPS and PDR, the number of endoscopically detected polyps, and ANDR among colonoscopies. We defined a case with more than the BBPS of 5 as good preparation.

**Results:** A total of 3480 cases (60% male, mean age 66 years, 22% with positive fecal occult blood test, 52% for surveillance or screening, 26% for the other reasons) underwent colonoscopy. Among them, 84 patients with advanced colorectal cancer and 489 patients with the other reasons were excluded. Finally, a total of 2907 patients were enrolled in this study. PDR is 68% (1994/2907). Average BBPS was $7.1 \pm 1.5$ and good preparation was achieved in 94% of patients who showed significantly higher PDR than poor preparation (69.3% vs 58.1%, $p = 0.0042$) and more number of polyps ($2.0 \pm 0.04$ vs $1.2 \pm 0.2$, $p < 0.001$). However, PDRs seemed to reach the plateau more than the BBPS of 6. We divided into three groups based on the number of polyps (Group A: 1 to 2, Group B: 3 to 5, Group C: more than 6). ANDR of Group A, B and C were 18.4%, 37.9% and 69.8%, respectively. There was significantly increased ANDR with the number of polyps (Odds ratio: Group A:B:C = 1 :2.7 :10.2).

**Conclusion:** Excellent bowel preparation (BBSP > 7) may not be necessary to increase the PDR but good bowel preparation significantly increases the number of endoscopically detected polyps that contributed to higher ANDR.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1491 THE OUTCOMES OF COLD POLYPECTOMY ARE NOT INFERIOR EVEN WHEN IT WAS PERFORMED BY LESS EXPERIENCED ENDOSCOPISTS: A PROPENSITY SCORE MATCHED CASE CONTROL STUDY OF 1,000 POLYPS

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**Introduction:** Cold polypectomy (CP) is a widely accepted technique used to remove diminutive and small colorectal polyps, because of its safety and convenience. However, the difference of outcomes of CP by endoscopists' experiences remains unclear.

**Aims & Methods:** The aim of this study was to assess safety and efficacy of CP that performed by less experienced endoscopists. A total of 451 consecutive patients who underwent colonoscopy from April 2014 to May 2015 had CP for 1,000 polyps. We retrospectively divided objectives into two groups according to endoscopists' experience; experienced group (Group E) with more than 2,000 cases of colonoscopy and less experienced group (Group LE) with less than 1,000 cases. All endoscopists participated in an intensive training program on endoscopic diagnosis of colorectal polyp including Sano NBI classification by an expert endoscopist before starting to perform CP. CP was applied for polyps less than 10 mm diagnosed as an adenoma endoscopically. We applied cold snare polypectomy (CSP) for small (6–9 mm) polyps, and cold forceps polypectomy (CFP) for diminutive (1–5 mm) polyps, respectively. Clipping was carried out only in case of continuous arterial bleeding after CP. We compared base-line characteristics (sex, number of polyps per patients and polyp size), type of cold polypectomy procedure (CFP or CSP) and outcome measurements including adverse events (immediately/delayed perforation, delayed bleeding required endoscopic intervention), polyp histology and technical success (En-bloc resection rate, lateral resection margin) between two groups. Multivariate analysis was performed to identify risk factors for unclear lateral resection margin using logistic regression model, and cases and propensity score-matched control was chosen on a one-to-one basis by adjusting risk factors revealing independence for unclear lateral resection margin other than endoscopists' experience.

**Results:** In Group E, there were significantly more female (34% vs 28%, $P = 0.003$), more polyps per patient (5.4 vs. 3.5, $P < 0.01$) and larger polyp (4.8 mm vs. 4.0 mm, $P < 0.01$) than Group LE. CSP was more frequently performed in Group E (60% vs. 32%, $P < 0.01$). Perforation and delayed bleeding did not occur at all. The proportion of lesion pathologically diagnosed as high grade dysplasia was 0.15% and 0.20% in Group E and LE, respectively ($P = 0.26$). En-bloc resection rate was accomplished in 96% of patients in both groups. Although unclear lateral resection margin was significantly lower in Group E (49% vs 57%, $P = 0.019$), there was no significant difference of rate of unclear margin (48% vs 51%, $P = 0.18$) after adjustment of size of polyp, number of polyps per patients and type of cold polypectomy procedure between both groups.

**Conclusion:** This large-scale retrospective study demonstrated that clinical outcomes of CP performed by less experienced endoscopists were as good as that by experienced endoscopists.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1492 A NOVEL ANTI-CD24 MONOCLONAL ANTIBODY, HUMANIZED AND AFFINITY MATURATED, FORTARGETING GASTROINTESTINAL CANCERS

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**Introduction:** CD24 is a cell-surface heavily glycosylated GPI-anchored protein. We had previously shown that CD24in an important player in the multistep process of GI carcinogenesis (Gastro 2006, Clin Can Res 2007, Can Res 2008). The creation of chimeric, humanized or fully human antibodies was a major breakthrough and led to a wave of USFDA-approved antibodies

**Aims & Methods:** Aim: To further improve the efficacy of the humanized anti-CD24 mAb by increasing its binding strength and therebygenerating a novel therapy tool for GI malignancy Methods: From murine to humanized, unarmed and conjugated, small derivatives and full IgG antibodies wererecombinantly engineered. The antibody genes were recovered, amplified and cloned into appropriate vectors. Thenthe vectors were introduced into a host (mammalian and *E. coli*) and adequate amounts of functional antibody wereachieved. Sequence analysis of the CDR loops was the base for library designing. Affinity maturation was performedin two-steps selection (CDR walking) and by using phage display technique. The binding of the different derivativeswere evaluated on full Glycan array in which more than 70 sugar moieties were printed.

**Results:** In vivo antibody targeting and accumulation within a CD24 positive tumor and its excess clearance wasclearly demonstrated using live imaging device (Maestro Cri device). High-affinity antibodies were selectedand created from combinatorial phage-displayed antibody libraries that contain varying degrees of diversity atrandomized positions. A chosen matured clone was isolated and showed higher binding strength (1.8x10–8), compared to the parental murine and humanized Abs. The matured antibody showed selective recognition andbinding to the CD24 antigen which proves that the genetic manipulations carried out did not affect its properties. Itsstability was enhanced following the maturation process, as well as its pharmacokinetics parameters which showed along serum half-life.The matured antibody mediates ADCC (antibody-dependent cell cytotoxicity), 75% oftarget cell lysis was demonstrated. Combined treatment with standard chemotherapy and natural products, such as monoterpenes (terpinen-4-ol), showed significant reduction in cell viability (90% cell death). Binding of anti-CD24 Ab to glycan microarray could not be detected while high binding intensities were observed where the whole CD24 protein was printed, indicating that the antibodies bind to the core peptide and not to its sugar residues.

**Conclusion:** Targeting CD24 may be a promising treatment for GI malignancies in combination with chemotherapy and natural agents. The resulted matured humanized anti-CD24 mAb proved to be more effective than the murine parental Ab. The long serum half-life is desirable as it would decrease the need for repetitive injections.

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## P1493 MONOTERPENES: A NOVEL AND PROMISING THERAPEUTIC AGENT, FOUND IN ESSENTIAL OILS, FOR HUMAN COLORECTAL CANCER

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**Introduction:** Monoterpenes are major secondary metabolites present in plants, and known to beassociated with the plant defense mechanisms. Many anticancer drugs that are currently in clinical use have beenisolated from plant species. Monoterpenes are such promising agents. Sobrerol was discovered as an oxidationproduct of terpenes while Carveol was isolated from spearmint oil. They exhibit anti-parasitic, neuromodulatory, andanticancer activities. It was demonstrated that carveol and sobrerol have chemopreventive activity against mammarycancer when fed during the initiation phase. We have shown that terpinen-4-ol, an additional monterpene, has animpressive synergistic inhibitory effect, in vitro and in vivo, when combined with commonly used chemotherapeuticagents and biological tools.

**Aims & Methods:** Aim: To study the antitumor effects of monoterpenes, such as carveol and sobrerol, and their mechanism of action invarious types of GI malignancies, alone and in combination with several chemotherapeutic and biological agents. Methods: Carveol and sobrerol were administrated alone or combined with standard anti-CRC agents including, oxaliplatin, fluorouracil (5-FU), cetuximab and bevacizumab. Killing effects were measured qualitatively by lightmicroscopy and quantitatively using the MTT assay. Subcutaneous tumors were produced by injection of 5x106 ofCRC cell lines into nude mice. When the tumors reached a dimension of 5 mm treatment was initiated.

**Results:** Carveol and sobrerol induce a significant growth inhibition of CRC cell lines, including HCT116, HT29 andSW480, in a dose-dependent manner. The synergistic growth inhibitory effects on cancer cell proliferation were impressive.

**Conclusion:** The use of plant-derived anticancer substances alone and in combination with chemotherapeutic orbiological agents for treating various types of cancer is promising, with a synergetic efficacy that allow a lowerconcentration of chemotherapy and biological agents that can not only increase efficacy but can minimize toxicity aswell. Clinically important the Monoterpenes restore the activity and efficacy of cetuximab in ras mutated tumors.

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## P1494 THE VALIDITY OF COLORECTAL ESD FOR LARGE COLORECTAL TUMORS IN A GENERAL HOSPITAL

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**Introduction:** Colorectal ESD has still not been widely performed for large colorectal tumors, because of the high frequency of complications such as postoperative bleeding and perforation.

**Aims & Methods:** To evaluate the validity of ESD for large colorectal tumors, 245 patients who underwent colorectal ESD in Omori Red Cross Hospital from 2012 April to 2016 March were retrospectively analyzed. We divided the patients into Group A (12–49 mm) and Group B (≧50 mm). The two groups were compared with respect to their clinical backgrounds, tumor characteristics and complications.

**Results:** For the 245 cases, 227 cases (92.7%) were assigned to group A ($69.0 \pm 10.7$ years old), and 18 cases (7.3%) were assigned to Group B ($69.6 \pm 15.2$ years old). The tumor location was C32/A48/T50/D25/S31/R41 in Group A and C1/A1/T2/D1/S3/R10 in Group B. The lesion size and procedure time were $25.5 \pm 8.2$ mm and $37.8 \pm 33.5$ min in Group A, and they were $71.4 \pm 23.3$ mm and $126.0 \pm 60.4$ min ($p < 0.01$) in Group B. Fibrosis during ESD (non/mild/severe) was 187/36/4 in Group A and 10/6/2 in Group B ($p = 0.0055$). En bloc resection rates were 100% and 17/18 (94.4%) ($p = 0.073$).

Complication rates were 2/227(0.9%) and 0%. These two cases in Group A were perforation (one of these cases required emergency surgery). Histology was adenoma121/Tis88/T1a9/T1b9/others0 in Group A and adenoma2/Tis12/T1a0/T1b3/others1 in Group B. Curative resection rates were 96.0% in Group A and 88.9% in Group B ($p = 0.189$). With respect to the postoperative course, there were also no differences in WBC, a number of having a high fever (≧38°C), and taking a painkiller between two groups.
**Conclusion:** Despite of higher fibrosis rates or longer procedure time, the benefits of ESD for large colorectal tumors (Group B) are almost similar to Group A.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1495 SAFETY, EFFICACY AND PROBLEMS OF COLD SNARE POLYPECTOMY FOR SMALL COLORECTAL NEOPLASMS

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**Introduction:** Cold snare polypectomy (CSP) has been performed worldwide as a safe endoscopic treatment for colorectal neoplasms compared with hot snare polypectomy (HSP). However, it is considerably difficult to evaluate pathological examination, post-cold polypectomy because of failed polyp retrieval and unclear cut margin. Incomplete resection is one of the most common causes that results in local recurrence after endoscopic treatment for colorectal neoplasms. The aim of this study is to assess the safety, efficacy and problems of CSP compared with HSP for small colorectal neoplasms.
**Aims & Methods:** We retrospectively analyzed a total of 1,239 lesions in consecutive 702 consecutive patients who underwent CSP or HSP for non-pedunculated polyps up to 10 mm in size at the Akashi Medical Center, Hyogo, Japan, from May 2013 to February 2016. When lesions were found, we used chromoendoscopy and narrow band imaging (NBI) in all cases and included a magnifying examination if magnifying endoscopy was possible to use. Endocrip was performed when the oozing did not decline even after one minute of observation in CSP, on the other hand in HSP it depended on operator's decision. We retrieved the transected polyps for histopathological evaluation. We aimed to evaluate patient characteristics, clinicopathological features of the polyps, complications, polyps retrieval, and pathological complete resection rates for neoplasm lesions in both groups. Furthermore, we assessed the influence of snare type (traditional snare or dedicated snare for CSP) on the effectiveness in the CSP group. The data were statistically analyzed.
**Results:** CSP was performed on 817 lesions in 458 patients while HSP was performed on 442 lesions in 244 patients. Patient characteristics and clinicopathological features of the polyps did not show significant differences in both groups. Polyp size was significantly smaller in CSP group compared with the HSP group ($3.63 \pm 1.31$ vs $5.06 \pm 2.23$ mm, $p < 0.01$). The retrieval rate for polyps was significantly lower in the CSP group compared with HSP group at 91% and 96%, respectively, $p = 0.0007$. In addition, pathological complete resection rate of the neoplasm lesions was also significantly lower in CSP compared with HSP at 67% and 74%, respectively, $p = 0.0217$). Delayed bleeding requiring endoscopic hemostasis was seen in one case in each groups. The rate of using endoclip was significantly lower in CSP compared with HSP at 3% and 19%, respectively, $p < 0.01$. In the CSP group, snare type had no influence on the pathological complete resection rate at 66% and 67%, respectively, $p = 0.960$.
**Conclusion:** CSP tended to conduct for significantly smaller lesions compared with HSP in this study. Although there was under such a situation, as the rate of using endoclip was significantly lower in CSP than in HSP, delayed bleeding with endoscopic hemostasis was seen in only one case and perforation was not observed. Thus, CSP could be a safer and more convenient method for small colonic neoplasia compared with HSP. On the other hand, polyp retrieval and pathological complete resection rates were significantly lower compared with HSP. Consequently, these findings highlight the importance of meticulous inspection of the remnant tumor via endoscopy after CSP to avoid unnecessary future local recurrence.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1496 DO FUNCTIONAL GASTROINTESTINAL DISORDERS ORIGINATE IN THE GUT RATHER THAN THE BRAIN? EVIDENCE FROM A 12 YEAR PROSPECTIVE POPULATION-BASED STUDY OF A PREDOMINANT GUT-BRAIN PATHWAY IN OVER 50%

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**Introduction:** Mood disorders are present in most patients with functional gastrointestinal disorders (FGIDs) including irritable bowel syndrome (IBS) and functional dyspepsia (FD) leading them to be conceptualized as brain gut syndromes. In contrast, recent evidence suggests gut dysfunction (and gut symptoms) may occur first in a subset and only later do mood disorders follow, implying a predominant gut-brain syndrome. [1] In others, mood disorders may occur first followed by gut dysfunction (a brain-gut syndrome).[1]
**Aims & Methods:** We aimed to re-analyse data from a prospective 12 year cohort study [2] in order to calculate the proportion of people with IBS and / or FD who have a brain-gut and a gut-brain syndrome as this was not estimated in the published paper. Participants ($n = 1775$) were a random population sample from Penrith, Australia who responded to a valid survey on functional gastrointestinal symptoms, psychological factors and quality of life via the SF-12 in 1997 and agreed to be contacted for future research. Of these $n = 1002$ completed the 12-year follow-up survey (response rate = 64%). Among those followed, $n = 44$ met Rome II criteria for new onset IBS and $n = 23$ for new onset FD, respectively. Controls ($n = 626$) did not meet Rome II criteria for any functional gastrointestinal disorder (FGID). Clinically elevated levels of psychological distress (anxiety and depression) were defined as a score of ≥4 out of 12 on the valid Delusions Symptom States Inventory (DSSI). A brain gut syndrome was defined as those people who were free of a FGID at baseline but who had clinically elevated levels of anxiety and/or depression at baseline and who then met criteria for a new onset FGID 12 years later. A gut-brain syndrome was defined as those people meeting criteria for a FGID at baseline who later reported clinically elevated levels of anxiety and/or depression at the 12 year follow up.
**Results:** Among the sample ($n = 1002$), we found a subgroup of 143 people who had either functional gut problems or psychological problems (but not both) at baseline. Of these 67 (47%) recorded psychological distress before a FGID diagnosis, implicating a brain-gut syndrome. In contrast we found 76 (53%) recorded a FGID before psychological distress suggesting a gut-brain pathway. People classified as having a brain-gut syndrome were significantly more likely to be younger and have signficantly higher baseline scores on neuroticism, anxiety, depression but a significantly lower baseline score on the mental but not physical functioning subscale of the SF-12 (Table 1). There was a trend for more females in the brain-gut versus gut-brain group (67.7%, $n = 42$ vs. 50%, $n = 38$, $P = 0.1$) but this was not significant.

Univariate discriminators of brain-gut and gut-brain syndromes

| | Brain- Gut Group (Mean, Std Dev) | Gut-Brain Group (Mean, Std Dev) | P Value |
|---|---|---|---|
| Age | 42.4 (12.9) | 45.8 (11.8) | 0.03 |
| Neuroticism | 6.3 (3.1) | 4.5 (3.1) | 0.002 |
| Extroversion | 5.9 (2.9) | 5.5 (2.8) | 0.3 |
| Anxiety | 5.6 (2.5) | 1.7 (1.1) | <0.0001 |
| Depression | 3.3 (2.7) | 0.7 (0.9) | <0.0001 |
| Physical QoL | 48.6 (10.2) | 49.6 (9.3) | 0.6 |
| Mental QoL | 42.4 (12.9) | 45.8 (11.8) | 0.03 |

**Conclusion:** These data further support the bidirectional nature of the brain-gut pathway in FGIDs and confirms an earlier study that there is a major subset of people (>50%) with FGIDs who have their disorder begin in the gut. We conclude the gut can probably drive psychological alterations in the FGIDs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1497 ALTERED FUNCTIONAL CONNECTIVITY ASSOCIATED WITH DISTURBED INTEROCEPTIVE AWARENESS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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**Introduction:** Visceral hypersensitivity is a core characteristic of irritable bowel syndrome (IBS), likely related to altered processing of sensory stimuli along the brain-gut axis. In particular, interoception (i.e. the process responsible for monitoring and processing visceral sensations and internal stimuli and likely associated with pain and visceromotor control) might play a pathogenic role in IBS. Neuroimaging studies in IBS patients demonstrated structural and functional alteration of brain areas involved in bodily representation. Only a few studies investigated brain functional connectivity through resting-state functional magnetic resonance imaging (rs-fMRI), with inconsistent results.
Aims & Methods:
**Aims:** 1) To investigate functional connectivity within the network involved in self-bodily consciousness; 2) To explore possible relationships between changes in functional connectivity and clinical and psychological measures, including measures of mood and anxiety.
**Methods**: We studied 19 patients aged 22 to 76 years (13 F, 6 M, mean age $39.6 \pm 13.5$ years) with diagnosis of IBS according to Rome III criteria, and 26 healthy controls (16 F, 10 M, mean age $40.1 \pm 15.3$ years). All subjects underwent rs-fMRI, carried out at 3 Tesla (Trio, Siemens Medical Systems, Erlangen, Germany). All patients completed a battery of questionnaires assessing gastrointestinal symptoms, interoceptive awareness (Self-Awareness Questionnaire), attitudes associated with hypochondriasis (Illness Anxiety Scale and Hypochondriac Yale-Brown Obsessive Compulsive Disorder- Modified), anxiety (State Trait Anxiety Inventory) and depression symptoms (Beck Depression Inventory- II). Patients underwent also a neuropsychological examination.
**Results:** 1) We observed two opposite patterns of functional connectivity. First, we found a cluster of significant inverse correlation between hypocondriasis score and rs-fMRI-determined connectivity between posterior cingulate cortex and left supramarginal gyrus, extending into the adjacent superior temporal gyrus; 2) We found a significant and positive correlation between interoception score and rs-fMRI-determined connectivity between left anterior ventral insula and two clusters located in supramarginal gyrus bilaterally; 3) Behavioural data showed that IBS patients had both depression and anxiety symptoms, but also underlined the correlation between depressive symptoms and levels of interoceptive awareness.
**Conclusions:** 1) The psychological and behavioural characterization of our IBS patients demonstrated a definite hypochondriac aspect with high interoceptive awareness; 2) In IBS patients functional connectivity data highlighted an "abnormal network synchrony" (i.e., a functional alteration in specific brain areas involved in interoceptive awareness) in the absence of structural and micro-structural changes; 3) The results of this study might shed new light on the complex pathophysiology of IBS and provide novel targets for efficient treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1498 VISCERAL HYPERSENSITIVITY REMAINS STABLE OVER TIME IN PATIENTS WITH IBS, BUT WITH INDIVIDUAL FLUCTUATIONS

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**Introduction:** Visceral hypersensitivity in IBS, measured with a rectal barostat, has been suggested to be a phenomenon that is abolished due to habituation at repeated investigations (Naliboff 2006).
**Aims & Methods:** We aimed to investigate the stability of rectal sensitivity in patients with IBS who had undergone a previous rectal barostat study (index investigation) and also assess variations in symptom pattern and severity in relation to rectal sensory function. IBS patients, who had previously been investigated with a rectal barostat, were included. All patients underwent a second rectal barostat study using the same protocol as the index investigation (isobaric phasic distensions; 30 s duration, 30 s rest; 5 mmHg increments). Thresholds for first sensation, urge to defecate, discomfort, and pain were determined during the distensions. Visceral hypersensitivity was defined as a pain threshold < 31 mmHg (5th percentile healthy controls). Symptoms were characterized by use of questionnaires; GI Symptom Rating Scale-IBS (GSRS-IBS), Hospital anxiety and depression scale, Visceral sensitivity index (VSI), and Symptom Checklist-90-Revised.
**Results:** In all, 27 subjects (17 Female) were included, mean age at index investigation 41, mean 10 yrs difference the new investigation (range 8–12 yrs). Pressure sensory thresholds were unchanged comparing the index study with the new one; perception (7.3 (new) vs 9.9 (old) mmHg $p = 0.09$), urge to defecate (13.5 vs 15.9 mmHg $p = 0.1$), discomfort (22.7 vs 24.9 mmHg $p = 0.4$), and pain (36.9 vs 37.9 mmHg $p = 0.7$). At the index, 8/27 patients had visceral hypersensitivity of which 4 were now reclassified normosensitive, and 7 from normo- to hypersensitive at the new investigation, meaning that 11/27 patients were hypersensitive at follow-up. Nine patients had increased pain thresholds (3–28 mmHg) at the new investigation, and 17 had decreased (1–17 mmHg). Total GSRS-IBS score and the individual symptoms remained unchanged, and no association between change in GI symptom severity and change in perception thresholds were seen ($p > 0.05$). There was no difference in anxiety or depression (HAD scale, $p > 0.05$ for both), no difference in the total IBS-QoL score (53 vs 47.5 $p > 0.05$), and no difference in somatization (SCL-90 R, 1.1 vs 0.4, $p > 0.05$). We also analysed the difference in sensory thresholds and correlated with the difference in symptoms, however no statistical correlation was found ($p > 0.05$ for all).

Differences in GSRS-IBS score, Data presented as mean (SD)

| Domain | New investigation | Index investigation |
|---|---|---|
| Total GSRS-IBS score | 2.3 (1.1) | 2.1 (0.8) |
| Pain GSRS-IBS score | 3.1 (1.5) | 3.3(1.5) |
| Bloating GSRS-IBS score | 3.1 (1.6) | 3.5 (1.4) |
| Constipation GSRS-IBS score | 2.2 (1.7) | 2.6 (1.5) |
| Diarreha GSRS-IBS score | 2.7 (1.4) | 3.0 (1.5) |
| Satiety GSRS-IBS score | 1.4 (1.2) | 1.7 (1.0) |

**Conclusion:** Visceral hypersensitivity and GI symptoms were stable at the group-level over 8–12 years in this cohort of IBS patients, even though individual fluctuations were noted. Our findings contradict previous findings that have indicated that visceral hypersensitivity is an unstable trait in IBS patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1499 IRRITABLE BOWEL SYNDROME WITH POSTPRANDIAL SYMPTOM OCCURRENCE IS ASSOCIATED WITH A POSTPRANDIAL WORSENING OF VISCERAL HYPERSENSITIVITY

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**Introduction:** Irritable bowel syndrome (IBS) is characterized by recurrent abdominal discomfort or pain associated with an alteration of bowel habits. Other symptoms, not included in the diagnostic criteria, but similarly bothersome are frequently present (1). The occurrence of symptoms in IBS during the day is variable (2), but meal ingestion may cause their worsening in more than 60% of patients (3). The occurence of postprandial symptoms in IBS raises a great deal of speculative interest on pathophysiological grounds.
**Aims & Methods:** The aim of our study was to evaluate visceral sensitivity in fasting condition and after the ingestion of a meal in a subgroup of IBS patients with postprandial symptoms in comparison with healthy volunteers (HV). 85 patients with IBS (mean age $34 \pm 6$ yrs), diagnosed according to Rome III criteria (IBS-C = 55; IBS-D = 28; IBS-M = 12) and a group of 20 HV comparable for age and gender were enrolled. Postprandial exacerbation of symptoms was present in 40 IBS. After an overnight fast, all the subjects underwent the recto-sigmoid barostat test. Basal and post prandial (200 Kcal, 200 ml liquid meal) recto-sigmoid sensitivity thresholds were determined by sequential ramp distensions with patients reporting their sensation on a 0–6 scale (4). The presence and severity of abdominal symptoms (abdominal pain or discomfort, abdominal distention, bloating, flatulence, nausea, belching, postprandial fullness, satiety, epigastric burning) were evaluated by VAL while fasting and every ten minutes for sixty minutes postprandially.
**Results:** Both mean fasting and postprandial perception threshold in IBS with postprandial symptoms and without postprandial symptoms were significantly lower than HV (fasting: $4.9 \pm 3.0$, $5.3 \pm 3.8$ and $9.8 \pm 3.5$ mmHg; postprandial: $4.5 \pm 3.8$, $4.4 \pm 4.7$, $9.6 \pm 3.9$ mmHg, respectively, ANOVA $p < 0.001$). Postprandial values were not significantly different than fasting values in all

the groups. As expected, in both IBS groups, mean fasting discomfort threshold was significantly lower than in HV (IBS with postprandial symptoms $12.8 \pm 5.2$ mmHg, IBS without postprandial symptoms $13.1 \pm 3.8$ mmHg; HV $20.2 \pm 5.8$ mmHg, ANOVA $p < 0.001$). Between the two subgroups of IBS, this parameter did not show a significant difference. On the contrary, only in IBS patients with postprandial symptoms was the postprandial discomfort threshold significantly lower than fasting values (IBS with postprandial symptoms $9.1 \pm 5.6$ mmHg; $p < 0.001$ vs fasting; IBS without postprandial symptoms $12.1 \pm 5.6$ mmHg; NS vs fasting; HV $19.5 \pm 4.3$ mmHg, NS vs fasting). Finally, only in IBS patients with postprandial symptoms was there a significant increase of postprandial abdominal discomfort and bloating ($2.88 \pm 1.87$ and $4.33 \pm 2.19$, respectively). None of the patients suffered from dyspeptic symptoms.

**Conclusion:** In a subgroup of IBS patients, the postprandial worsening of visceral hypersensitivity may cause postprandial symptom occurrence. Further studies are needed to clarify the neural pathway responsible for this alteration.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1500 FEMALE IBS PATIENTS WITH VISCERAL HYPERSENSITIVITY DEMONSTRATE ALTERED AMYGDALA CONNECTIVITY WITHIN THE DEFAULT MODE NETWORK

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**Introduction:** Increased visceral sensitivity plays a key role in the pathophysiology of Irritable Bowel Syndrome (IBS) as a disorder of the brain-gut axis. Previous brain imaging studies revealed altered neural responses to expected or delivered visceral stimuli in hypersensitive compared to normosensitive IBS patients. At the same time, evidence supporting a role of fear and arousal in altered pain processing in IBS is accumulating with amygdala as a key region. Resting state imaging allows the investigation of task-independent connectivity between regions that may be involved in altered modulation of visceral afferent signals. While changes in functional connectivity within networks involved in sensory and affective processing have previously been reported in IBS, the possible contribution of visceral sensitivity to altered amygdala resting-state connectivity in IBS has not yet been studied.

**Aims & Methods:** Our aim was to address differences in resting-state connectivity in IBS patients with visceral hypersensitivity compared to normosensitive IBS and healthy controls (HC) with a focus on the amygdala as a key structure involved in emotion and fear processing. Forty-one women with IBS and 20 female HC were included. Rectal sensory thresholds were determined with a barostat and patients were subdivided into a group with increased (hypersensitive IBS, $N = 21$) and a group with normal sensitivity (normosensitive IBS, $N = 20$) based on HC thresholds. Resting state fMRI data was acquired using a 1.5T MRI scanner with a single-shot gradient-echo EPI sequence ($TR = 3s$) to effectively cover the whole brain. Group independent component analysis (ICA) was used within the full sample and sensorimotor, executive control, salience and default mode networks were derived using spatial regression. Within these networks, amygdala was most strongly related the default mode network (DMN). Between-group differences in functional connectivity between amygdala and DMN were carried out using region-of-interest analyses and the mean connectivity within the amygdala was extracted for each participant and correlated with visceral sensitivity.

**Results:** Hyper- and normosensitive IBS differed significantly in rectal thresholds for maximum tolerable distension ($47 \pm 1$ mmHg vs. $30 \pm 2$ mmHg, $p < .001$). Two-sample t-tests revealed enhanced positive connectivity of the amygdala with DMN in hypersensitive compared to normosensitive IBS ($t = 5.06$, $p < .001$). The strength of amygdala connectivity correlated significantly with rectal pain thresholds ($r = -.58$, $p < .001$). DMN-amygdala connectivity did not differ between IBS as a whole and HC or in comparisons of either patient subgroup with HC.

**Conclusion:** Our findings support enhanced connectivity between amygdala and DMN at rest in IBS patients with visceral hypersensitivity. These findings provide a possible link between visceral hypersensitivity and central mechanisms involved in emotional arousal and call for more work on the central fear network in IBS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1501 CHOICE OF RECTAL BAROSTAT PROTOCOL AFFECTS CLASSIFICATION OF SENSORY FUNCTION AND PREDICTION OF SYMPTOM SEVERITY IN IBS

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**Introduction:** Rectal barostat studies are widely used to assess visceral sensory function in patients with irritable bowel syndrome (IBS). However there are no studies comparing the optimal protocol to distinguish visceral hypersensitivity from normal bowel sensitivity. This study compares two protocols and their ability to distinguish between patients and healthy controls, and if the sensitivity measures associate differently with GI symptom severity.
**Aims & Methods:** We retrospectively included patients with irritable bowel syndrome (diagnosed according to Rome II criteria) that previously underwent rectal balloon distention at our center as a component their evaluation. Cohort 1 included 369 patients with IBS (38.5 ± 12.5 (mean ± SD) years; 279 females) and 35 healthy controls (36 ± 11 years; 27 females), cohort 2 included 153 patients with IBS (34.5 ± 12 years; 105 females) and 66 healthy controls (31.5 ± 9 years; 41 females). IBS symptoms were characterized by use of IBS-SSS and GSRS-IBS questionnaires. Cohort 1 underwent a rectal barostat study with isobaric phasic distensions (30 s duration, 30 s rest; 5 mmHg increments, maximum 70 mmHg) (Posserud 2007). Sensory thresholds and the perceived intensity of unpleasantness and pain were determined during the last 10 seconds of each distension. Cohort 2 underwent a rectal barostat study with ramp inflation for sensory thresholds (4 mmHg steps, 1 min/step) followed by random phasic distensions (12, 24, 36, 48 mmHg) for intensity of gas, urge, discomfort and pain (Cremonini 2005). The fifth percentile for pain thresholds in healthy controls was used as cutoff for defining hypersensitivity in both cohorts.
**Results:** There was a significant difference between the cohorts in age (cohort 1 presented first) 38.5 (SD 12.5) vs 34.5 years (SD 12, $p < 0.05$). No difference was seen in sex, body composition, psychiatric illness, oro-anal transit time, or IBS subtype ($p > 0.05$ for all). IBS patients in cohort 1 had lower thresholds for first sensation and pain ($p < 0.001$ for both) compared with cohort 2. However, the perceived intensity of pain was higher at the closest comparable pressure levels in cohort 2 ($p < 0.001$ for all) and differed from their controls ($p < 0.05$). There was also a significant difference in the proportion of patients classified as having hypersensitivity in cohort 1 vs 2; for pain 43% vs 7%, urge to defecate 23.5% vs 7.5%, discomfort 47.5% vs 15%, and altered rectal perception for at least one sensory threshold 60% vs 19% ($p < 0.001$ for all). Overall, the protocol used in cohort 1 showed a better correlation with perceived IBS symptoms. Patients with hypersensitivity for at least one sensory threshold in cohort 1 were more likely to have more severe diarrhea, bloating, pain, and early satiety (GSRS-IBS scores $p < 0.05$ for all) and to have a GSRS-IBS score $> 3$ ($p < 0.05$) compared with patients in cohort 2.
**Conclusion:** IBS patients evaluated with a rectal barostat test using isobaric phasic distensions perceived less pain at comparable pressures than patients where ramp inflation and a random phasic distension protocol was used. The isobaric phasic distension protocol was also better at predicting GI symptom severity.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1502 ADULT COLONIC HYPERSENSITIVITY CORRELATES WITH JUVENIL INTESTINAL DYSBIOSIS IN NEONATAL MOTHER SEPARATED MICE

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**Introduction:** Visceral pain is a diffuse and stabbing sensation which may be associated with functional gastrointestinal disorders such as Irritable Bowel Syndrome (IBS). This complaint is a crucial feature because of its significant impact on patients' quality of life and lack of efficient therapies. Recent studies revealed dysbiosis associated to IBS suggesting a long term impact of the intestinal microbiota on inflammation, but also on colonic hypersensitivity (CHS). In addition, such patients also suffered from stress-related psychiatric disorders including anxiety and depression. In this context, the aim of this work was to determine the impact of a neonatal maternal separation (NMS) paradigm on intestinal microbiota and to correlate dysbiosis to stress-induced CHS.
**Aims & Methods:** Stress-induced CHS was obtained by NMS: after birth, wild-type C57Bl/6J pups were isolated from their mother from P2 to P14 and CHS was assessed using a non-invasive technique based on a colorectal distension (CRD) coupled to intraluminal colonic pressure recording on 8- and 12-weeks old mice. Fecal pellets were collected directly from mice at week 3 (just before weaning), week 4, 6, 8 and 12. Next generation sequencing (NGS) of 16S genes were performed by Illumina on fecal samples of NMS mice compared to control non-handled (NH) mice.
**Results:** NMS induced a significant CHS at week 8 and week 12 in some mice (NMS sensitized: NMS-S) while some littermates did not shown an increased sensitivity to CRD test (NMS non-sensitized: NMS-NS). Interestingly, CHS was associated with a marked intestinal dysbiosis in NMS-S mice compared to NH and NMS-NS littermate mice from week 3 to week 12. This modification of fecal microbiota composition was characterized by a decreased relative abundance of some bacterial species with a beneficial effect on CHS such as *Bifidobacterium longum* or *Faecalibacterium prausnitzii*.
**Conclusion:** These results shown a direct involvement of intestinal microbiota in stress-induced CHS suggesting that targeting intestinal microbiota could be a new therapeutic approach to modulate CHS and associated abdominal pain in patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1503 ALTERED RESTING STATE FUNCTIONAL CONNECTIVITY IN ROSTRAL ANTERIOR CINGULATE CORTEX IN IBS WITH COMORBID ANXIETY

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**Introduction:** Anxiety can contribute to altered brain processing of visceral signals in Irritable Bowel Syndromes (IBS) as a disorder of brain-gut communication.[1] The rostral anterior cingulate cortex (rACC) has been associated with both anxiety and pain perception and has been recently proposed to be a key region in mediating anxiety-related enhancement of pain.[2] The objective of the present study was to identify changes in resting state functional connectivity in rACC as a measure of synchronicity among brain regions in IBS patients and to assess its relation to anxiety.
**Aims & Methods:** Resting state FMRI data were acquired on 22 healthy females and 41 female IBS patients using a 3T MRI scanner. A single-shot gradient-echo EPI sequence was used to effectively cover the whole brain with a TR of 2 s. Data were preprocessed using standard procedures in SPM8. Group independent component analysis was used to identify a resting state network that spatially correlated to the rACC. The mean functional connectivity within the rACC was extracted for each subject. The IBS patients were sub-divided based on Hospital Anxiety and Depression Scale (HADS) into patients with ($IBS^+$, $n = 22$) and without ($IBS^-$, $n = 19$) clinically relevant anxiety, and a one-way ANOVA was used to assess overall group differences in rACC functional connectivity among the controls, $IBS^+$and $IBS^-$.
**Results:** A trend-level between-group difference in functional connectivity was noted within the rACC and between rACC and mid- and posterior cingulate cortex (MCC/PCC) ($F_{(2,61)} = 2.85$, $p < 0.065$). Post-hoc tests indicated that the controls had higher functional connectivity than the $IBS^+$ patients ($p < 0.025$). Similarly, the $IBS^-$ patients were also observed to have higher functional connectivity than the $IBS^+$ patients ($p < 0.09$). No difference was noted between the healthy controls and the $IBS^-$ patients ($p > 0.6$).
**Conclusion:** Anxiety, as a common comorbidity in IBS, contributes to dysfunctional communication between brain regions involved in affective pain control.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1504 ACHALASIA SYMPTOM RESPONSE AFTER POEM SEGREGATED BY HIGH-RESOLUTION MANOMETRY SUBTYPES

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**Introduction:** To evaluate the symptomatic response of peroral endoscopic myotomy (POEM) for achalasia subtypes segregated by high-resolution manometry (HRM).
**Aims & Methods:** Treatment-naive subjects with achalasia referred for POEM were followed in this observational study. Chicago criteria designated achalasia subtypes (subtype I: no esophageal pressurization; subtype II: panesophageal pressurization in more than 20% swallows; subtype III: premature contractions in more than 20% swallows). Symptom questionnaires assessed symptom burden before and after POEM on five-point Likert scales as well as Eckcardt score were recorded. Data were analyzed to determine predictors of symptom response.

**Results:** 45 achalasia patients (44.1 ± 14.0years, 46.7% female) fulfilled inclusion criteria, 6 patients with subtype I, 34 patients with subtype II, and 5 patients with subtype III achalasia. Upon follow-up 1.5 years after POEM, Eckcardt score declined from 8.0 (7.0) 9.0) to 1.5 (1.0 3.0) (P = 0.000); these were similar across achalasia subtypes. There was no statistical difference between the incidence of symptom for dysphagia, both solid and liquid, and regurgitation and chest pain. While solid dysphagia was the main symptom in each achalasia subtypes. Post-POEM symptom scores for dysphagia, both solid and liquid, regurgitation and chest pain were significantly lower than pre-operation in type II patients [solid dysphagia:16.0(12.0,16.0) vs 2.0(1.0,8.3)(P = 0.000), liquid dysphagia: 2.0(0.0,5.0) vs 0.0(0.0,0.0)(P = 0.001), regurgitation:9.0(7.0,10.5) vs 0.0(0.0) 1.0)(P = 0.000), chest pain: 2.0(0.0,9.0) vs 0.0(0.0,1.8)(P = 0.005)]. Post-POEM symptom scores for solid dysphagia, and regurgitation were significantly lower than pre-operation in both type I and III patients [type I: solid dysphagia :16.0(12.0) 16.0) vs 1.0(1.0) 5.3)(P = 0.027), regurgitation:10.5(8.3) 12.0) vs 0.0(0.0) 1.5)(P = 0.038); type III: solid dysphagia:16.0(14.0) 16.0) vs 0.0(0.0) 5.0)(P = 0.042), regurgitation: 9.0(7.5) 12.0) vs 0.0(0.0) 0.0)(P = 0.041)]. On multivariate analysis, female gender was positively correlated with symptom scores for solid dysphagia, regurgitation and chest pain, drinking history was positively correlated with symptom scores for Eckcardt score, liquid dysphagia and chest pain, while 4sIRP in solid swallow was negatively correlated with symptom scores for liquid dysphagia and 4sIRP in liquid swallow was positively correlated with symptom scores for both solid and liquid dysphagia.
**Conclusion:** When a uniform approach is utilized, symptomatic outcome are different across achalasia subtypes. Female, drinking history, low 4sIRP in solid swallow and high 4sIRP liquid swallow may predict worse POEM outcome.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1505 PROTEIN DISULFIDE ISOMERASE A3 MEDIATED IMMUNE DYSFUNCTION OF DENDRITIC CELLS IN THE COLON OF RATS WITH VISCERAL HYPERSENSITIVITY

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**Introduction:** The molecular mechanisms of visceral hypersensitivity are still poorly understood. We had already proved that antigen presenting dendritic cells (DCs) mediated abnormal immune response play a cardinal role in the formation of visceral hypersensitivity in rats. Protein disulfide isomerase A3 (PDIA3) is involved in the process of antigen presentation by loaded onto major histocompatibility complex I (MHC I) proteins. Our previous work found that stress can significantly induce high level of protein disulfide isomerase A3 (PDIA3) in the colonic mucosa in IBS rat model. Therefore, in the present study, we established a stress related model with visceral hypersensitivity and try to identified the relationship between PDIA3 and dentritic cells.
**Aims & Methods:** Twenty male rats were chosen to established a stress related IBS model by intraperitoneally infused with corticotropin releasing factor (CRF). All rats underwent abdominal withdrawal reflex (AWR) to evaluate visceral sensitivity. Western blotting was used to determine the protein expression of PDIA3 in colonic mucosa, DCs from mesenteric lymph nodes were numbered by double labeling immunofluorescent staining of either CD11c (marker of dendritic cells in rats) and PDIA3. The rat mesenteric lymph nodes dendritic cells (MLNDCs) were obtained by the technique of magnetic bead sorting. The expression of MHCI was tested by the technique of flow cytometry and western blot. Splenic CD8+Tcells were isolated and purified by magnetic label-based technique. The capacity to stimulate CD8 + T cells was evaluated by mixed lymphocyte reaction (MLR).
**Results:** In comparison to controls, all rats in the model group manifested higher visceral sensitivity ($p < 0.05$). Western blotting showed that protein expression of PDIA3 was up-regulated in colonic mucosa in IBS rats ($P < 0.05$), both CD11c-positive dendritic cells and PDIA3-positive cells observed under fluorescence microscopy were significantly increased in the IBS group compared with the control group ($P < 0.05$), in addition, the number of CD11c/PDIA3-positive cells in the IBS group was statistically more than in the control group in mesenteric lymph nodes ($P < 0.05$). Compared with control group, MLNDC from model group expressed high level of MHCI, and had the ability to attract and stimulate CD8+ T cell proliferation.
**Conclusion:** High level of protein disulfide isomerase A3 observed in dendritic cells could enhance the antigen presentation by up regulating the expression of MHCI on the surface of MLNDC, which may lead to the immune activation of CD8 + T cell and the generation of visceral hypersensitivity of IBS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1506 INTERACTIONS BETWEEN THE ENDOGENOUS OPIOID AND CANNABINOID SYSTEMS IN THE GASTROINTESTINAL TRACT ARE CRUCIAL IN THE DEVELOPMENT OF TOLERANCE TO OPIOIDS

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**Introduction:** Peripherally restricted opioids were proposed as promising therapeutics in diarrhea-predominant irritable bowel syndrome (IBS), as they eliminate diarrhea and alleviate abdominal pain. The development of tolerance to opioids is an important limitation of prolonged opioid administration. Previous studies have shown that tolerance to morphine develops in the ileum, but not in the colon. Moreover, it was reported that the co-activation of opioid (OR) and cannabinoid (CB) receptors reduced the development of tolerance related to the analgesic effect of opioids.
**Aims & Methods:** The aim of our study was to validate a new research tool that could be employed to study the development of tolerance to opioids in the GI tract and to characterize the interactions between OR and CB receptors in this process. To assess the development of tolerance to opioids, an in vitro opioid-induced withdrawal response (WR) protocol was used. Isolated segments of mouse ileum were mounted in organ baths and challenged with naloxone ($10^{-6}$M) to induce WR. WR was expressed as a change of smooth muscle tension prior to and immediately after exposure to naloxone. To validate this in vitro method, selective OR and CB agonists (both $10^{-6}$M): morphine and WIN 55,212–2, respectively, were used.
The involvement of OR and CB receptors interaction in tolerance development was evaluated using, as pharmacological tools, mixed agonists: salvinorin A (SA) and its derivative PR-38, which is devoid of action in the central nervous system (both at $10^{-6}$M). To determine the involvement of CB receptors, AM251, a CB1 receptor antagonist was used. The effect of PR-38 on upper GI tract motility, the geometric center of GI tract and gastric emptying in vivo, was characterized in mice pretreated chronically with PR-38 (5 mg/kg, i.p., injected every other day for 14 days) and compared with animals treated acutely with PR-38 (5 mg/kg, i.p.).
**Results:** In the ileum exposed to morphine, naloxone induced a significant WR; in the tissue exposed to WIN 55,212–2 WR was not observed. There was no WR in the ileum exposed to SA or PR-38; however, the CB1 antagonist AM251 evoked a significant naloxone-induced WR in the ileum exposed to SA or PR-38. Acute and chronic administration of PR-38 produced a significant slowing effect on upper GI transit, reduced gastric emptying and lowered geometric center of GI tract in comparison to control.
**Conclusion:** The dual activation of OR and CB receptors using PR-38 significantly reduced tolerance to opioids in the GI tract. These results indicate that mixed OR/CB receptors agonists may be effective agents in prolonged therapy of GI disorders and that further research is warranted.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1507 ESTROGEN RECEPTOR BETA AGONIST, LY3201, AMELIORATES HIGH FAT DIET INDUCED COLONIC NEUROPATHY AND MYOPATHY

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**Introduction:** Increased consumption of High Fat Diet (HFD) can induce several gastrointestinal motility disorders due to enteric neurons loss and reduction in neurotransmitter's synthesis; the most affected neurotransmitters seems to be vasoactive intestinal peptide (VIP), acetylcholine and nitric oxide. It is well known that estrogen can have protection on neurons via estrogen receptor Beta (ER$\beta$). The aim of our study was to investigate the role of LY3201, a selective ER$\beta$ agonist, on HFD induced colonic neuropathy and myopathy.
**Aims & Methods:** Nine male mice were fed a HFD (60% kcal from fat) for three months. Five of them were treated with pellet containing LY3201 and the other 4 with a vehicle pellet for 7 days. Colons were subjected to histological processing and immunohistochemistry was performed to evaluate myenteric neuron's expression of Er$\beta$, VIP, neuronal nitric oxide synthases (nNOS) and choline acetyltransferase (ChAT). The data were compared between the groups using non parametric t-test.
**Results:** Er$\beta$ is expressed in the neurons of the myenteric plexus. The thickness of muscle layer in LY3201-treated group was greater than in vehicle (mean 144.48 ± 20.92 vs 88.53 ± 18.13). The density (cell number/colon length) of colonic myenteric neurons (Neun-positive) in treated group was increased compared to the vehicle (respectively mean 29.85 ± 9.82; 6.93 ± 3.42; $p < 0.004$). In LY3201-treated group, the density of Sox2-positive cells (a subset of neural progenitor cells) was higher (mean 34.76 ± 9.53 treated; 8.94 ± 1.53 vehicle; $p < 0.0017$). Moreover the drug increased Chat (mean 14.8 ± 2.6 treated; 1.9 ± 0.9 vehicle; $p < 0.003$)and nNOS (mean 11.6 ± 2.1 treated; 2.3 ± 0.8 vehicle; $p < 0.0065$) expression while didn't affect VIP significantly.

**Conclusion:** LY3201 increased thickness of the smooth muscle layer and the number of neurons and Sox2-positive cells in the myenteric plexus. Probably it can promote Sox2+ progenitor cells differentiating into neurons. Moreover LY3201 restored neuron's ability to produce neurotransmitters (nNOS/Chat) damaged by HFD. Thus LY3201, a selective ER$\beta$ agonist, can ameliorate HFD induced colonic neuropathy and myopathy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III – POSTER EXHIBITION**

### P1508 CLINICAL FEATURES OF ESOPHAGEAL ULCERS IN HIV-POSITIVE PATIENTS

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**Introduction:** Japan has an increasing population of people with human immunodeficiency virus-1 (HIV) infection. Esophageal ulceration is one of the most common complaints among HIV-positive patients, although esophageal ulceration can also be caused by Candida species, cytomegalovirus (CMV), and herpes simplex virus (HSV). Thus, idiopathic esophageal ulcers can be re-classified as being related to HIV infection after excluding the possibility of infections with pathogens that are also common among HIV-positive patients.
**Aims & Methods:** We retrospectively evaluated the clinical characteristics and endoscopic features of 40 HIV-positive patients with esophageal ulceration who underwent upper gastrointestinal endoscopy between September 1997 and March 2016 at the Department of Gastroenterology and Hepatology, Osaka National Hospital.
**Results:** The median age of the 40 patients (39 men) was 41 years (range, 23–70 years). The average HIV-RNA titers were 1,120,000 copies/mL and the average CD4+ cell count was 58/$\mu$L. The most common presentations of the esophageal ulcers were odynophagia (n = 14, 35%), epigastric or chest pain (n = 13, 32.5%), anorexia (n = 3, 7.5%), anemia (n = 2, 5%), and hematemesis or melena. Among the 40 patients, 34 patients (85%) had ulcers that were oblong with a sharply demarcated ''punched-out'' appearance, 7 patients (17.5%) had ''geographic ulcers'' resembling the islands of an archipelago and 30 patients (75%) had multiple ulcers. The most common sites were the middle and lower thoracic esophagus (n = 15, 37.5%), the lower thoracic esophagus (n = 11, 27.5%), the middle thoracic esophagus (n = 6, 15%), and the upper thoracic esophagus (n = 2, 5%). Moreover, 24 patients had CMV-related ulcers, 2 patients had HSV-related ulcers, 1 patient had a CMV- and HSV-related ulcer, and 9 patients had idiopathic esophageal ulcers (the causes were unclear in 2 patients, because of insufficient investigation). Before antiretroviral therapy (ART), patients with Candida esophagitis received antifungal therapies, and patients with CMV or HSV infection received antiviral therapy (valganciclovir, ganciclovir, or foscarnet). Patients with idiopathic esophageal ulcers were only treated using ART. All cases of idiopathic esophageal ulcers exhibited symptom improvement, and endoscopy after the start of ART revealed reductions in the size and depth of the ulcers (or disappearance). Interestingly, we identified HIV infection in 6 patients after the endoscopy.
**Conclusion:** Esophageal ulceration can help diagnose HIV infection, and it is important to detect the infectious agent(s) that caused the esophageal ulcers. However, clinicians should also be aware of the possibility of idiopathic esophageal ulcers. Our results indicate that ART was effective for treating idiopathic esophageal ulcers, and that endoscopy helped diagnose HIV infection.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1509 IMPAIRMENT IN ACTIVITY OF DAILY LIVING IS A RISK FACTOR FOR HIGH MEDICAL CARE COST IN PATIENTS WITH NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

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**Introduction:** Despite recent progress of health care standard, non-variceal upper gastrointestinal bleeding (NVUGIB) is still a common and life-threatening disease. It sometimes requires intensive care, thus it would have a big impact on medical care cost. However, little is known about risk factors for increased medical care cost in NVUGIB patients.
**Aims & Methods:** The aim of this study is to clarify characteristics of NVUGIB patients requiring high medical care cost. This was a retrospective study from a tertiary care hospital. Patients who underwent endoscopic hemostasis due to NVUGIB were included in this study. Patients with low risk for re-bleeding (Forrest classification IIb or III) based on retrospective review of recorded endoscopic images were excluded. Medical care cost was calculated in reference to the ''Diagnosis Procedure Combination'' which is diagnosis-dominant case-mix system in Japan. We defined the cutoff value of high medical care cost as its first quartile. Univariate logistic regression model was used to determine an association between high medical care cost and various clinical factors [age, gender, usage of antiplatelet/anticoagulant drug, Glasgow-Blatchford score, activity of daily livings (ADL) before admission]. ADL was assessed according to Katz-6 score (Katz, et al, *Gerontologist* 1970). It is calculated considering whether the patients were possible six basic performances in daily life (bathing, dressing, toileting, sitting and standing, necessity of incontinence products, and eating). If patients couldn't perform these items by themselves, each items scored 1. Scores of each item were summed up and total score ranges 0 (fully maintained) to 6 (completely impaired). We divided the eligible patients into maintained ADL (Katz-6 score: 0) and impaired ADL (Katz-6 score more than 1) groups. Multivariate logistic regression analysis was performed among factors indicated p-value less than 0.20 in univariate analysis. The exchange rate from Japanese Yen to USD was 120.
**Results:** A total of 128 consecutive patients admitted due to NVUGIB between April 2012 and March 2015. Mean age was 68.6 ± 15.4 years old and male-to-female ratio was 2: 1. Median medical care cost was 5,323 USD [IQR 3.661 – 8.172 USD]. There were 13 patients (10%) in impaired ADL group. In univariate analysis, age and impaired ADL before admission revealed significant association with high cost. Of these, impaired ADL was an only independent risk factor [Odds Ratio 15.3 (95% C.I. 2.49 – 183)] in multivariate analysis. Katz-6 score positively also correlated with medical cost ($r = 0.23$, $p < 0.01$).
**Conclusion:** Impairment in ADL before admission was an independent predictor for high medical care cost with NVUGIB patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1510 EFFICACY AND SAFETY OF FERRIC CARBOXYMALTOSE IN THE MANAGEMENT OF IRON-DEFICIENCY ANEMIA IN PATIENTS WITH GASTROINTESTINAL AND LIVER DISEASE

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**Introduction:** Iron deficiency anemia (IDA) is common in gastrointestinal and liver disease. Oral iron is often ineffective and poorly tolerated while conventional intravenous (IV) iron is effective but requires repeated infusions. Ferric carboxymaltose (FCM) is a novel intravenous iron preparation that can be administered in single doses. In this retrospective study we aimed to evaluate efficacy and safety of FCM in a cohort of patients with IDA related to gastro-intestinal disease.
**Aims & Methods:** We analyzed 63 consecutive patients admitted to our day-care unit because of IDA from January 2014 to September 2015. Anemia (defined as Hb < 13 g/dl in men, Hb < 12 g/ dl in non-pregnant women) was classified as IDA if ferritin value was < 30 ng/ml. There were 27 (43%) patients with Inflammatory Bowel Disease, 17 (27%) with liver cirrhosis, 4 (6%) with celiac disease, 15 (24%) with other G-I disease. Clinical-demographic characteristics were registered on a dedicated database. We evaluated Hb, serum iron and ferritin values at baseline, after 2 and 8 weeks. FCM was administered by intravenous infusion of 500 mg in 15 minutes. We also evaluated the need for a second infusion of FCM and number of blood transfusions at baseline and after iron therapy. Safety was also assessed.
**Results:** By a single infusion of FCM, we obtained a mean increase of 1.3 g/dl in Hb values (Hb levels at baseline 9.5 ± 1.2 g/dl, 10.8 ± 1.5 g/dl at week 2) ($p < 0.001$). Significant increases in mean levels of serum iron (31 ± 23 at baseline, 60 ± 33 $\mu$g/dL at 2 weeks, D 27 µg/ dl; $p < 0.001$) and ferritin (21.6 ± 47 at baseline, 126 ± 85 ng/mL at 2 weeks, D 105 ng/ml; $p < 0.001$) were also observed. A second infusion of FCM was necessary in 30% of patients. 11 patients (17%) had required at least one tranfusion before FCM treatment while only 5 patients (8%) needed transfusions after FCM. Only one adverse event was observed (skin rash). FCM was well tolerated also in 4 patients with a previous history of anaphylactoid reaction to iv iron.
**Conclusion:** A single infusion of FCM effectively improves Hb and iron status in patients with IDA due to GI disease regardless of etiology. Safety profile was excellent even in patients with liver disease and those with a previous history of allergic reaction to ev iron sucrose. The use of FCM reduces the impact of treatment on everyday life and work productivity and allows a more efficient utilization of hospital resources. Safety in patients with liver disease should be confirmed in larger series for the potential risk of iron overload.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1511 PEPTIC ULCER BLEEDING - DOES ETIOLOGY INFLUENCE CLINICAL OUTCOME?

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**Introduction:** With the declining prevalence of *Helicobacter pylori* (Hp) infection, polymedication and the increase in the average life expectancy, the epidemiology of peptic ulcer (PUD) has changed. Recent epidemiological studies report an increase in idiopathic PUD (I-PUD) incidence. The clinical impact (rebleeding and 30 day mortality) of this data is not fully understood. [1–2]
**Aims & Methods:** In patients with upper gastrointestinal bleeding (UGIB) secondary to PUD, we performed a comparison between the characteristics and clinical outcomes of the different etiologies of PUD, with the main focus on I-PUD. Retrospective analysis of all admissions secondary to PUD bleeding in a

tertiary center, between 2009 and 2014. We divided patients into 4 groups according to etiology: PUD associated to Hp (Hp-PUD); drug induced PUD (D-PUD: non-steroidal anti-inflammatory drugs, antiplatelet, anticoagulants); combined PUD (C-PUD: Hp and drug-induced PUD) and I-PUD (without Hp or drug history). Our main endpoint was rebleeding, defined as: 1) objective evidence of UGIB, with hemodynamic instability and Hb decrease $\geq$ 2g/dL; 2) or a requirement for more than 3 units of blood transfusion for more than 3 days.
**Results:** We identified 381 patients with a mean age of 71 years and with a mean length of hospitalization of 7 days. The PUD was classified as: D-PUD: 41.2%; Hp-PUD: 24.1%; C-PUD:19.7% and I-PUD 15%. Rebleeding happened in 20%, surgery for hemostatic control in 8% and in hospital mortality was 7%. There was a statistically significant difference according to the etiology of PUD for age ($p = 0.019$), Age Adjusted Charlson Comorbidity Index (ACCI; $p < 0.000$), Alcoholism ($p = 0.010$), length of hospitalization ($p < 0.000$) and rebleeding ($p = 0.001$). No statistically significant difference was identified between the groups ($p > 0.05$) for the variables: hemodynamic instability, location (gastric or duodenal), high-risk location (small gastric curvature or posterior wall of the bulb), size of PUD, Forrest classification, number of red blood cell (RBC) units transfused, need for surgery and in hospital mortality. In multivariate analysis besides Forrest $\geq$ 2B ($p < 0.000$; OR = 10.137), I-PUD ($p = 0.049$; OR = 1.972), duodenal location ($p = 0.014$; OR = 2.280), high-risk location ($p = 0.009$; OR = 3.017) and ACCA $\geq$ 6 ($p = 0.000$; 3.011) were independent risk factors for rebleeding.

| | I-PUD N = 57 | Hp-PUD N = 92 | D-PUD N = 157 | C-PUD N = 75 | P value |
|---|---|---|---|---|---|
| Age (years) | 68 (16.66) | 67 (18.69) | 73 (13.69) | 71 (15.5) | **0.019** |
| Gender (m/f) | 43/14 | 68/24 | 114/43 | 53/22 | 0.934 |
| ACCI | 5 (3.06) | 4 (2.26) | 6 (3.14) | 6 (3.20) | **0.000** |
| Past PUD | 13 | 19 | 29 | 7 | 0.158 |
| Smoking | 15 | 15 | 28 | 14 | 0.463 |
| Alcoholism | 10 | 11 | 10 | 2 | **0.010** |
| Hemodynamic instability | 21 | 26 | 33 | 24 | 0.085 |
| Location (Gastric/Duodenal) | 26/31 | 35/57 | 73/84 | 28/47 | 0.420 |
| High-risk location | 9 | 10 | 15 | 8 | 0.642 |
| Forrest $\geq$ 2B | 43 | 53 | 103 | 55 | 0.074 |
| Estimated PUD size (mm) | 12.9 (7.1) | 13.6 (8.3) | 11.5 (6.6) | 11.4 (6.5) | 0.092 |
| Hb (g/dL) at admission | 8.9 (2.54) | 8.1 (2.65) | 8.4 (2.68) | 8.1 (2.29) | 0.209 |
| Number of RBC units | 2 (2.38) | 2 (1.55) | 2 (1.48) | 2 (1.30) | 0.078 |
| Length of hospitalization | 9 (8.32) | 4 (2.70) | 8 (7.20) | 6 (3.69) | **0.000** |
| Rebleeding | 18 | 6 | 37 | 16 | **0.001** |
| Mortality | 7 | 4 | 13 | 4 | 0.272 |

**Conclusion:** In our sample we identified a high prevalence of I-PUD (15%). Different PUD etiologies presented distinct characteristics and clinical outcomes. In our sample I-PUD was an independent risk factor for rebleeding.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1512 RISK OF PEPTIC ULCER BLEEDING ASSOCIATED WITH HELICOBACTER PYLORI INFECTION, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS, LOW-DOSE ASPIRIN IN PEPTIC ULCER DISEASE: A CASE-CONTROL STUDY


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**Introduction:** The association of *Helicobacter pylori* (*H. pylori*) infection, non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose aspirin in the risk of peptic ulcer bleeding (PUB) has not yet been established. Also, it remains unclear whether aspirin and NSAIDs increase the risk of bleeding from gastroduodenal ulcers.
**Aims & Methods:** This study aimed to determine the risk of PUB associated with *H. pylori* infection, NSAIDs and low-dose aspirin in peptic ulcer disease (PUD). This case-control study included 300 hospitalized patients with PUB and age, sex-matched 300 patients with PUD diagnosed endoscopically at our institution from 2012 to 2015. Adjusted odds ratio (AOR) for the risk of PUB were calculated by logistic regression analysis.
**Results:** The study included 300 cases of PUB and 300 controls of PUD. 57.7% of cases and 52.3% of controls had *H. pylori* infection ($P = 0.18$). In multivariate analysis, low-dose aspirin (AOR, 5.96; $P = 0.0001$), NSAID (AOR, 4.6; $P = 0.0001$), smoking (AOR, 1.98; $P = 0.006$) and alcohol intake (AOR, 1.85; $P = 0.012$) increased risk of PUB compared to PUD. No significant interactions were observed between *H. pylori* infection and NSAIDs or low-dose aspirin use in logistic regression analysis.
**Conclusion:** Both NSAIDs and aspirin are independent risk factors for bleeding in patients with PUD, however, there were no additive effects between low-dose aspirin or NSAID use and *H. pylori* infection. Therefore, preventive strategies for bleeding are warranted in patients with PUD taking low-dose aspirin and NSAIDs continuously.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1513 MEDICAL VERSUS COMBINED THERAPY OF PEPTIC ULCERS WITH ADHERENT CLOTS


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**Introduction:** The optimal therapeutic approach of peptic ulcers with adherent clots, Forrest IIb Classification, is not consensual. The results of the studies so far performed are somewhat contradictory and both isolated medical treatment and medical treatment combined with endoscopic treatment are considered on the European Society of Gastrointestinal Endoscopy guidelines[1].
**Aims & Methods:** We aimed to compare evolution and prognosis of patients with Forrest IIb ulcers approached with isolated medical treatment versus combined treatment (medical and endoscopic). All patients with Forrest IIb gastric or duodenal ulcer, diagnosed between January 2010 and December 2015 were admitted. A clot was considered adherent when resistant to endoscopic aspiration and/or irrigation, with no signs of active bleeding. All patients that underwent any method of endoscopic haemostasis (injection, thermal and/or mechanic) were included in the endoscopic treatment group.
**Results:** We selected 58 patients (69.0% male; mean age 67.0 ± 13.9 years), 43.1% ($n = 25$) in the isolated medical treatment and 56.9% ($n = 33$) in the combined treatment group. Demographic and clinical features were identical between both groups ($p > 0.05$). The recurrence rate was 9.1% ($n = 3$) in the combined treatment group Vs. 28.0% ($n = 7$) in the medical treatment group; $p = 0.059$. Patients of the combined treatment group had shorter duration of hospitalization (5.9 ± 3.2 Vs. 7.8 ± 3.8 days; $p = 0.042$) and required less transfusion (1.2 ± 2.4 Vs. 2.7 ± 2.8 units of blood; $p = 0.031$). The surgery requirement (6.1% Vs. 20.0%; $p = 0.221$), bleeding-related mortality (3.0% Vs 4.0%; $p = 0.841$) and all-cause mortality (12.1% Vs. 24.0%; $p = 0.302$) did not reach statistical difference between both groups. There was an association between syncope at admission, Blatchford score and ulcer size and the recurrence rate ($p < 0.05$).
**Conclusion:** Combined treatment, medical and endoscopic, of Forrest IIb ulcers is associated with shorter hospitalization, less transfusion requirement and a tendency towards recurrence rate reduction.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1514 FIRST EXPERIENCE IN THE DEPLOYMENT OF HEMOSPRAY AS SALVAGE THERAPY IN GASTROINTESTINAL BLEEDINGS


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**Introduction:** Gastrointestinal bleeding represents the main indication for emergency endoscopy and, albeit a plethora of potential interventions, yields a mortality rate of up to 10%. Lately several hemostatic powders, such as "Hemospray", have been released in order to increase the success rates during emergency endoscopy.
**Aims & Methods:** During a study period of 15 months, all emergency endoscopies were evaluated, in whom Hemospray application was performed to achieve hemostasis. The aim of this study was to report short- and long-term hemostasis rates, outcome and adverse events after Hemospray application.
**Results:** In 488 emergency endoscopies, Hemospray was applied during 35 examinations (7.17%) in 27 patients (19 males). Hemospray was used after previous endoscopic treatment in 21 examinations (60%) and in 14 (40%) as salvage therapy.
Short-term success was reached in 34 of 35 applications (97.1%), while long-term success was documented after 23 applications (65.7%).

Recurrence of bleeding was found particularly in malignancy and ulcerative lesions involving larger arteries. But even in these patients, short-term hemostasis enabled hemodynamic stabilization and planning of further definitive interventions.
One major adverse event (2.8%) occurred with gastric perforation immediately after Hemospray application, requiring surgery.
**Conclusion:** Hemospray achieved a short-term hemostasis in virtually all cases. Intermittent hemostasis gives further essential time to improve intensive care treatment. The long-term effect is mainly determined by the type of bleeding source, involvement of larger arteries, and in combination with a hampered coagulation system. But, even in these cases, patients benefit from a hemodynamic stabilization and consecutive interventions optimized conditions.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1515 APPRAISING AND IMPROVING JUNIOR DOCTORS MANAGEMENT OF ACUTE VARICEAL UPPER GI BLEEDS: A QUALITY IMPROVEMENT PROJECT

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**Introduction:** Acute gastrointestinal bleeding is a medical emergency. Some 44% of bleeds are caused by peptic ulcer disease but the most severe haemorrhage and highest mortality is seen amongst those with bleeding oesophageal or gastric varices[1]. Competent triage and assessment are cornerstones of its initial management, with emphasis on identifying sick patients with life-threatening hemodynamic compromise, and then initiating appropriate and timely resuscitation being of paramount importance in the patient's outcome. In a national audit, variceal bleeding accounted for just over 10% of all UK admissions, with approximately two-thirds having a previous history of variceal bleeding and just fewer than 50% presenting outside normal working hours[2]. The average mortality of the first episode of variceal bleeding is reported to be up to 20%, with studies confirming a 2–3 fold increase in mortality amongst inpatients[3]. Therefore it is paramount that all junior doctors involved in acute admissions and inpatient care are able to recognise and manage suspected variceal bleeds appropriately.
**Aims & Methods:** The primary aim of this project was to appraise and then to improve the knowledge, skills and confidence of junior doctors in caring for patients with upper gastrointestinal bleeds (UGIB), to ultimately improve patient safety and outcomes. This objective was achieved through initially identifying areas of weakness in junior doctor's knowledge of managing an acute variceal upper GI Bleed. The areas identified were then the basis of a later rolled out dedicated Foundation Year one (FY) and two teaching session on acute variceal bleeding. An initial questionnaire was distributed and completed by 67 junior doctors (FY1-FY2) at the University Hospitals of Leicester in November 2015, all with jobs involving the acute medical take and providing ward cover. The questions on the questionnaire were devised around a real life case scenario. Junior doctors were then asked a series of questions and their perceived confidence and knowledge was sampled in a range of key areas i.e. management pre and post endoscopy, senior support and escalation, blood transfusion targets, knowledge and confidence in activating the major haemorrhage protocol and use of risk stratification tools such as the Blatchford score. Following evaluation of the initial questionnaire results a dedicated teaching session on variceal bleeds was devised and rolled out to 65 FY1's and FY2's. Following the teaching session the junior doctor's perceived confidence and knowledge on management of variceal bleeds was then re-assessed in January 2016.
**Results:** Following introduction of the teaching session all junior doctors expressed improved confidence in managing variceal UGIBs- which improved from 8% to 41% of junior doctors feeling confident. Additionally there were significant improvements identified in all areas assessed. Notably; correct pre-endoscopic management improved to 94% (from 36%), selecting appropriate transfusion targets improved from 45% to 76%, knowledge and understanding of risk stratification scores and how to activate the major haemorrhage protocol improved to 88% and 94% respectively (from 3% and 30% respectively). With inappropriate pre-endoscopic use of proton pump inhibitors falling from 25% to 0% after the introduction of the teaching session. This clinically would translate to better patient care, safety and outcomes.
**Conclusion:** Adopting a focused teaching programme for junior doctors on the management of acute variceal bleeds designed around pre-identified areas of weakness has proven to increase both knowledge and confidence in its specific management. Junior doctor teaching on core medical emergencies such as UGIBs should perhaps be incorporated into Trust induction, to ensure junior doctors are as prepared as possible on their first day in clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1516 REBLEEDING RATE AND THE NEED FOR BLOOD TRANSFUSION IN PATIENTS WITH UPPER GASTROINTESTINAL TUMOR BLEEDING ARE HIGHER THAN IN PATIENTS WITH PEPTIC ULCER BLEEDING

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**Introduction:** The aim of this study was to compare peptic ulcer bleeding (PUB) with upper gastrointestinal tumor bleeding (UGITB) while placing special emphasis on the incidence, outcomes including thirty-day re-bleeding rate, mortality and the need for blood transfusion.
**Aims & Methods:** A total of 2198 patients referred to our Emergency Department with upper gastrointestinal bleeding (UGIB) were included in this prospective study during 5 years (from January 2008 till December 2012); 796 with PUB and 61 with UGITB, found during urgent upper GI endoscopy performed within 24 hours of admission.
**Results:** Cumulative incidence of UGIB was 126/100000 in a 5-year period. 796(36.2%) patients had PUB and 61 (2.8%) patients had UGITB. UGITB was most often found in the stomach (58/95%); the tumors were dominantly malignant (55/90%), most of them adenocarcinoma (48/87.3%). Median age for PUB was 67, and for UGITB 76 years($p < 0.01$). PUB and UGITB were more common in men (62.3% and 52.5%). Re-bleeding occurred more often in patients with UGITB(19.7% vs 9.7%, $p < 0.01$), but a higher number of patients with PUB required surgical intervention due to uncontrolled bleeding (5.9% vs 3.3% $p < 0.01$). Thirty-day mortality showed no difference between the two groups (5.2% vs 7.2%). Transfusion of red blood cells was administered more often in patients with UGITB (75.4% vs 49.5%, $p < 0.01$), while patients with PUB received comparably higher volumes of transfused red blood cells.
**Conclusion:** Patients with UGITB have higher re-bleeding rates, require surgical intervention less often, and are more often treated with blood transfusion than PUB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1517 HISTOACRYL ® THERAPY OF BLEEDING GASTRIC FUNDAL VARICES; THE EXPERIENCE OF TERTIARY CARE HOSPITALS

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**Introduction:** Gastric variceal bleeding is not only life threatening, also contributes to high rates of morbidity, recurrent hospitalizations
**Aims & Methods:** We aimed to evaluate the efficacy and safety of endoscopic injection of N-butyl-2-cyanoacrylate (NBCA) for treatment of bleeding gastric varices (GV). Methods: Analysis of prospectively collected data of a cohort of patients with GV who underwent endoscopy for the treatment of bleeding GV from April 2013 to September 2015. Patients with gastric variceal bleeding underwent endoscopic treatment with a mixture of NBCA and Lipiodol. The success of GV eradication was assessed by repeat endoscopy after 3 weeks of intervention. Successful hemostasis, rebleeding rate and complications were observed.
**Results:** The cohort consisted of 33 consecutive patients that had undergone NBCA injection for GV. The mean age was $51 \pm 10$ years. The mean follow-up was $16 \pm 8$ months and the most common cause for GV was hepatitis C related liver cirrhosis (51.5%). Child-Pugh score at presentation for was A-21%; B-79%, and median MELD score at admission was 10. A median mixture volume of 4.5 mL, in 1 to 2 injections, was used, with immediate hemostasis rate of 100% and early rebleeding rate 3.8%. Mortality rate was 3.8%. No immediate or long-term complications of NBCA injection occurred in any of these cases during the time of follow-up.
**Conclusion:** NBCA injection of GV is a safe and successful therapeutic intervention. Patients with very early rebleeding was at higher risk of death. A minimum of 2 endoscopic sessions is required to significantly decrease the risk of rebleeding.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1518 COMPARISON OF GLASGOW–BLATCHFORD SCORE, ROCKALL SCORE, AND AIMS 65 SCORE FOR PREDICTING UPPER GASTROINTESTINAL BLEEDING OUTCOME IN KOREA

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**Introduction:** Various clinical scoring systems have been developed and validated to predict the clinical outcomes in patients with upper gastrointestinal bleeding (UGIB), including the Glasgow–Blatchford score (GBS), Rockall risk score (RS), and AIMS65 score (AIMS65). Several studies have evaluated the predictive accuracy of these systems, but the results vary greatly, potentially limiting the generalizability of the findings.
**Aims & Methods:** We simultaneously compared the performance of these three scoring systems in predicting clinical outcomes in patients presenting with UGIB in Korea. We retrospectively evaluated 143 patients with UGIB who visited our emergency department between August 2013 and August 2014. The accuracy of the three scoring systems was compared using the area under receiver-operating characteristics curves. The primary outcome was the need for blood transfusion, clinical endoscopic intervention, or ICU admission, while the secondary outcomes were re-bleeding and 30-day all-cause mortality.
**Results:** The median patient age was 57.9 years, and 30.8% were women. The causes of UGIB were gastric or duodenal ulcer in 84 (59%) patients, esophageal/gastric varices in 32 (38%), Mallory-Weiss syndrome in 16 (11%), and unknown in 11 (8%). Eighty-seven (61%) patients required blood transfusion; 83 (58%), endoscopic interventions; and 5, (3.5%) surgical interventions. Thirteen (9.1%) patients experienced re-bleeding, and 6 (4.2%) died within 30 days of admission. The GBS outperformed the RS and AIMS65 in predicting the need for endoscopic intervention. Further, the GBS and RS outperformed the AIMS65 in predicting the need for transfusion as well as for ICU admission. No significant differences were found in the ability to predict re-bleeding rates and 30-day all-cause mortality among the three scoring systems.
**Conclusion:** The GBS was more effective and accurate than the RS and AIMS65 in predicting the need for clinical interventions in Korean patients with UGIB. Relatively, the AIMS65 may not be suitable for predicting clinical outcomes in Korean patients with UGIB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1519 OESOPHAGEAL HIGH RESOLUTION MANOMETRY IN CHRONIC INTESTINAL IDIOPATHIC PSEUDO-OBSTRUCTION

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**Introduction:** Oesophageal motility has been shown to be impaired in a minority of patient with chronic intestinal idiopathic pseudo-obstruction (CIIPO)[1] at traditional manometry. High resolution manometry (HRM) has improved the understanding of oesophageal pathophysiology in patients with oesophageal symptoms; however no studies have evaluated HRM in CIIPO patients.
**Aims & Methods:** To evaluate oesophageal motility with HRM in a cohort of patients with a confirmed diagnosis of CIIPO (chronic symptoms of obstruction, radiological evidence of distended gut with air-fluid levels and exclusion of any organic obstruction of the gut lumen). 15 CIIPO patients (6 M; 42 yrs; 29–50) who underwent HRM were retrospectively enrolled. 50 consecutive patients with oesophageal symptoms (dysphagia or typical/atypical oesophageal reflux symptoms) and a diagnosis of ineffective esophageal motility (IEM) served as a control group (18 M; 53 years; 39–68). Patients with secondary causes of chronic intestinal pseudo-obstruction, scleroderma, previous oesophageal and gastric surgery and eosinophilic oesophagitis were excluded. All diagnosis were based according to Chicago 3 Classification[2]. All patients underwent 10 single 5 ml water swallows (SS) and 2 multiple 10 ml rapid swallows (MRS) during HRM protocol. During MRS we evaluated the presence of motor inhibition, oesophagogastric pressure gradient (OGPG) as a measure of resistance to outflow and peristaltic reserve, which was considered to be present if MRS/SS Distal Contractile Index Ratio was > 1. Data are given as median and interquartile range (IQR). Mann-Whitney, Chi-squared or Fisher test were used when appropriate.
**Results:** All CIIPO patients had pathological HRM: one had type II achalasia, one oesophago-gastric junction obstruction (OGJO), one aperistalsis and 12 IEM. The 12 CIIPO patients with IEM were compared with our control group. No differences were seen between two groups comparing basal tone of the LES (9.5 mmHg; 6–16.5 vs 14 mmHg; 7–24), 4 second Integrated Relaxation Pressure (4 s IRP) (3 mmHg; 1.5–5 vs 3 mmHg; 1–6), Intrabolus Pressure (IBP) (14 mmHg; 3.5–17; 6 mmHg; 2–16) Distal Contractile Integral (DCI). Distal latency (DL) had a trend toward lower values in the CIIPO group compared to IEM group ($p = 0.07$) although no patients had DL < 4.5 sec. Number of failed waves (DCI < 100 mmHg.sec.cm) were similar between the two groups whereas number of ineffective waves (DCI < 450 mmHg.sec.cm) were higher in CIIPO group ($p = 0.001$). During MRS there were no differences considering motor inhibition (96% vs 90%) and OGPG (-0.5 mmHg; -2.8 to 1 vs 0.75 mmHg;-1.5 to 2.5) whereas MRS/SS DCI ratio ($p = 0.08$) and number of after contractions with MRS/SS DCI ratio > 1 ($p = 0.08$) had a tendency to be higher in CIIPO. Data are detailed in table 1.

**Table 1:** Data expressed as median; IQR

| | CIIPO (12) | IEM (50) | p value |
|---|---|---|---|
| **SS DCI (mmHg.sec.cm)** | 221; 136–471 | 324; 166–475 | 0.67 |
| **SS DL (sec)** | 6.9; 5.9–7.6 | 7.3; 6.6–8.2 | 0.07 |
| **SS waves with DCI < 450 mmHg.sec.cm** | 50% | 34% | 0.001 |
| **MRS DCI (mmHg.sec.cm)** | 560; 370–1151 | 469; 196–931 | 0.22 |
| **MRS/SS DCI ratio** † | 2.4; 2.2–2.9 | 1.5; 0.7–2.6 | 0.08 |
| **Waves with MRS/SS DCI Ratio >1**† | 9/10 (90%) | 28/45 (62%) | 0.08 |

†Evaluated in patients with presence of MRS after contraction, n = 10 in CIIPO and n = 45 in IEM.

**Conclusion:** HRM has identified oesophageal dismotility in all CIIPO patients, three major and 12 minor disorders. IEM of our CIIPO patients had similar HRM characteristics compared with patients with oesophageal symptoms with more ineffective waves in CIIPO patients, in which however peristaltic reserve was generally preserved as assessed during MRS.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1520 HLA-DQB1-INSERTION IN IDIOPATHIC ACHALASIA AND FIRST GENOTYPE-PHENOTYPE (GXP) STUDY USING HIGH-RESOLUTION MANOMETRY DATA

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**Introduction:** Idiopathic achalasia is a rare motility disorder of the esophagus (lifetime prevalence 1:10,000) characterized by impaired relaxation of the lower esophageal sphincter (LES) and disturbed esophageal peristalsis due to degeneration of inhibitory neurons within the myenteric plexus. The etiopathology is multifactorial with environmental and genetic factors being disease-associated, but the exact etiopathogenesis remains unknown. Recently a SNP rs28688207, located in HLA-DQ$\beta$ region on chromosome 6, leading to an 8-amino-acid insertion in the HLA-DQB1 subunit of the HLA-DQ receptor on the surface of antigen-presenting cells, has been identified as the strongest genetic risk variant for achalasia so far (Gockel et al., *Nat Genet*, 2014). With the introduction of high-resolution manometry (HRM), three subtypes of achalasia that have also different clinical presentation can be distinguished according to the Chicago classification: type I = 100% failed peristalsis, type II = panesophageal pressurization with ≥ 20% of swallows, type III = spastic contraction with ≥20% of swallows.
**Aims & Methods:** The aim of our study was to replicate the role of rs28688207 in achalasia pathogenesis in an independent case-control sample from the Czech Republic (204 patients, 220 controls). In addition, we performed the first genotype-phenotype (GxP) study to test whether rs28688207 is disease-associated to a particular HRM-subtype of achalasia. For the GxP analysis we used a cohort of patients including cases from the Czech Republic and Germany with detailed HRM data. From a total of 235 cases, 53 patients were diagnosed as achalasia type I, 147 as type II and 35 patients as type III according to the Chicago classification.

**Results:** Genotyping of rs28688207 in the case-control sample yielded a strong achalasia-association ($P = 1.22 \times 10^{-04}$). The frequency of 8-amino-acid insertion in HLA-DQB1 was present in 9.1% of patients while only in 2.7% of controls, which perfectly corresponds with the frequency seen in cases and controls in other countries in Central Europe. The GxP study revealed that rs28688207 is most prevalent in type I achalasia (11.3%) compared to type II (7.8%) and type III (4.3%), although this distribution was not statistically significant ($P = 0.266$).
**Conclusion:** Our results suggest that the 8-amino-acid insertion in HLA-DQB1 plays a pivotal role in achalasia etiopathogenesis. In addition, the insertion is most frequent in HRM-type I achalasia patients, followed by type II and III subsequently. It might be due to a small sample size of patients, that despite the clear trend of decreasing frequency from type I to type III achalasia, this was not statistically significant and larger number of patient samples with HRM data is needed in order to uncover whether the HLA-DQB1-insertion has an impact on achalasia also on the phenotypic level.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1521 IMPACT OF PER ORAL ENDOSCOPIC MYOTOMY ON ESOPHAGEAL HIGH RESOLUTION MANOMETRY PARAMETERS IN PATIENTS WITH ACHALASIA

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**Introduction:** Per oral endoscopic myotomy (POEM) is effective to treat achalasia. Despite the lack of controlled studies, it is frequently proposed as first line treatment.
**Aims & Methods:** We aimed at determining the effect of first-line POEM on esophageal contractile activity as defined with high-resolution manometry (HRM) and searching for predictive factors of response to treatment. Achalasia patients referred for POEM were included in this study. Patients with previous endoscopic or surgical treatment were excluded. HRM was performed before and 3 months after POEM. HRM protocol consisted of 30-s baseline recording without swallowing, 10 5-ml water swallows in supine position and multiple water swallow (MWS) test (200 ml free drinking) in seated position. The following manometric parameters were analyzed: esophago-gastric junction (EGJ) resting pressure, median integrated relaxation pressure (IRP) of 10 swallows, percentage of 5-ml swallows associated with pan-esophageal pressurization, and occurrence of pan-esophageal pressurization during MWS. Esophageal motility disorders were defined using the Chicago Classification version 3.0. Esophageal symptoms were assessed using the Eckardt score. Data before and after POEM are expressed as median (range) or percentage and compared using paired t-test or Chi2 test.
**Results:** Pre and post POEM data were available in 59 patients (37 males, mean age 57 years, range 27–84). Eight patients (13%) had type I achalasia, 40 (69%) type II, 5 (8%) type III and 6 (10%) a variant form (EGJ outflow obstruction with normal or weak esophageal contractions). Manometry catheter did not pass through the EGJ in 7 patients before POEM and 3 after POEM. Results before and after POEM are presented in the Table. After POEM, IRP was normal (<15 mmHg) in 49/56 patients (87%). Post POEM esophageal contractions were observed in all patients with achalasia variant, in 80% of patients with type III achalasia, in 58% of patients with type II but none of patients with type I achalasia. Post POEM esophageal contractions were premature (spasm) in 6 patients (3 type II, 2 type III, and 1 variant). POEM was successful (Eckardt score < 3) in 52 patients (88%) at 3 months. Response rate was 100% in type I achalasia, 90% in type II, 60% in type III and 83% in variant ($p = 0.16$). The percentage of patients with at least 20% of swallows associated with pan-esophageal pressurization after POEM tended to be higher in case of good response compared to failure (31% vs 0%, $p = 0.09$). No other factor (age, symptom severity at inclusion, EGJ resting pressure, IRP before and after POEM, post POEM esophageal contractions, and occurrence of pan-esophageal pressurization during MWS) was associated with POEM failure at 3 months.

| | prePOEM | post POEM | p |
|---|---|---|---|
| Eckardt score | 6 (2–11) | 1 (0–5) | <0.01 |
| EGJ resting pressure (mmHg) | 23 (4–78) | 7 (0–25) | <0.01 |
| IRP (mmHg) | 18 (5–50) | 7 (0–22) | <0.01 |
| Percentage of esophageal contractions with pan-esophageal pressurization | 60 (0–100) | 0 (0–100) | <0.01 |
| Percentage of patients with at least 20% of contractions with pan-esophageal pressurization, n (%) | 45 (76%) | 16 (27%) | <0.01 |
| Patients with pan-esophageal pressurization during MWS, n (%) | 37/47 (79%) | 7/52 (14%) | <0.01 |

**Conclusion:** POEM is responsible for a significant decrease of EGJ resting and relaxation pressure. Type III achalasia might be associated with a lower response rate; however the difference is not significant. Reappearance of esophageal contractions was observed in half of the patients without impact on treatment response. MWS might not be useful to predict response to POEM in patients with achalasia.
**Disclosure of Interest:** S. Roman: Consultant for Medtronic and Sandhill
F. Zerbib: consultant for Medtronic
F. Mion: Consultant for Medtronic
All other authors have declared no conflicts of interest.

## P1522 THE GASTRIC ACCOMODATION REFLEX STUDIED BY ULTRASOUND, MANOMETRY AND IMPEDANCEMETRY IN A PILOT STUDY

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**Introduction:** Upper gastrointestinal disorders affect up to 20% of adults in Western countries, and the origin of symptoms is poorly understood. We believe abnormal postprandial gastric accommodation to be of potential pathophysiological importance in patients with upper gastrointestinal symptoms.
**Aims & Methods:** We aimed to study normal physiology of the stomach and lower esophagus during and after food-intake by combining transabdominal ultrasound (US), a symptom score and multichannel high-resolution impedancemetry and manometry (HRIM) in a pilot study. After trans-nasal intubation, a HRIM-probe was distally positioned at angulus ventriculi, and a solution of 300 ml saline water with 67 g of glucose (255 kcal) was given. Our target variables (pressure changes, gastroesophageal reflux, stomach wall thickness and diameters, gastric wall stress and strain and upper gastrointestinal symptoms) enabled an evaluation of the postprandial adaptive accommodation reflex, and were recorded from shortly before until 30 minutes after the intake of fluid.
**Results:** 15 healthy volunteers (11 F/4 M, mean age 26.9 years), were included. All subjects accepted the 300 ml of fluid with few symptoms in general and minimal discomfort. Three subjects showed mild gastroesophageal reflux. At angulus ventriculi gastric pressure was significantly reduced from 6.2 mmHg (mean) shortly before intake, to a minimum of -1.2 mmHg after a median time of 75 seconds ($p < 0.0001$), rising to 3.9 mmHg at five minutes and to pre-intake-values within 20 minutes. The corresponding area and circumference showed a clear increase from shortly before intake (8.0 $cm^2$ (mean) and 11.3 cm respectively), to 14.1 $cm^2$ and 15.1 cm shortly after, both reaching a top level at five minutes, then slowly decreasing towards 30 minutes, but not to pre-intake-values. The corresponding calculated stress decreased significantly from 50.5 mmHg (mean) shortly before intake to 4.6 mmHg shortly after ($p = 0.0001$), subsequently rising to nearly pre-intake values after 5 minutes, and to 69.2 mmHg at 30 minutes.
**Conclusion:** US and HRIM enabled calculation of gastric wall stress and strain during the postprandial accommodation reflex, triggering few symptoms and scant reflux tendencies in healthy volunteers. We propose this to be a more physiological alternative to the barostat technique.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1523 STUDY OF DISTAL CONTRACTILE INTEGRAL IN INEFFECTIVE ESOPHAGEAL MOTILITY DIAGNOSIS AND ITS RELATION TO GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** High-resolution manometry has brought about a revolution in esophageal motility disorders, making it possible to identify new pressure patterns. Ineffective esophageal motility (IEM) is defined as ≥50% of ineffective swallows: Ineffective swallows can be classified as failed (Distal contractile integral (DCI) < 100 mmHgcmsg) or weak (DCI < 450). Historically IEM has been associated with gastroesophageal reflux disease (GERD), but it has not been proved whether it is the cause or the consequence.

**Aims & Methods:** The purpose of this study is to evaluate if a difference exists between the mean value of DCI in manometries with IEM diagnosis and normal manometries, as well as to check if patients with pathological pH monitoring had a DCI mean value lower than that of patients with normal pH monitoring. Retrospective and descriptive study of 116 high resolution manometries. Statistical comparison using $\chi^2$ test for normally distributed data and the Mann-Whitney U-test for non-normally distributed data. The data were analyzed using the program SPSS.20. A p value < 0.05 was established for signification

**Results:** 116 manometries were analyzed. 72 of them were measured on females (62.1%) averaging 53.65 year of age (range 23–81). According to the Chicago classification v3, 27 manometries (23.3%) reached IEM diagnostic criteria and 89 (76.7%) were normal. The mean of DCI readings in the normal manometry group was 1219.99 and the median was 1000 (range 442–4449). The mean DCI in the IEM group was 486.22 and the median was 409 (range 142–1527), p-value: < 0.01. 95th percentile of DCI in the IEM group was < 1454. 100 pH monitoring tests were carried out, and 59 of them were abnormal. In the 23 analysis carried out of a total of 27 patients in the IEM group, 13 (57%) showed pathological pH readings. There were no differences between pathological pH monitoring in the IEM group and that on the normal manometry group, p-value:0.786. The mean of DCI in patients with pathological pH monitoring was 978.24, the median was 834 (range 182–2346). The mean of DCI in patients with normal pH monitoring was 1249.93, the median was 981 (range 142–4449), p-value: 0.462

**Conclusion:** In this study we found significant differences in DCI values among IEM patients, as we conclude that patients with normal manometry readings have a higher DCI mean value than those in the IEM group. Therefore DCI may be an IEM diagnosis parameter. In this sample 95 percent of DCI values are below 1454; however, those values could have been influenced by 3 outliers. On the other hand, we didn't find significant differences in DCI between patients with pathological pH monitoring and patients with normal pH monitoring, which suggests that DCI is not connected with GERD. In addition, in our study the IEM group didn't have a higher incidence of GERD than the normal manometry group.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1524 DYSPHAGIA PATIENTS WITH NORMAL ESOPHAGEAL HIGH-RESOLUTION MANOMETRY: ASSESSING THE DIAGNOSTIC VALUE OF BREAD SWALLOWS

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**Introduction:** High-resolution manometry (HRM) is currently the gold standard technique to investigate esophageal motility in patients with dysphagia. However, with routine HRM procedure and use of Chicago classification, a group of patients with dysphagia are considered as being normal and dysphagia remains unexplained.

**Aims & Methods:** The aim of this study is to assess the diagnostic value of solid bolus swallows in patients with dysphagia and normal HRM. Patients having dysphagia and normal HRM studies during January-October 2015 were selected. Solid bolus swallows of bread (1cm$^3$ single bread swallows and/or a sandwich meal) followed the routine water swallows on HRM. Patients with a double high pressure zone, esophageal diverticulum or history of antireflux surgery were excluded.

The patients were categorised to symptomatic and asymptomatic groups based on having dysphagia reproduced on bread swallows. Hospital odynophagia and dysphagia questionnaire (HODQ) score, integrated relaxation pressure (IRP), distal contractile integration (DCI), distal latency (DL) and peristaltic abnormality during water swallows were investigated and compared between groups. ROC curve was used to identify the optimum level of sensitivity and specificity of the significant parameters in identifying patients who have a meaningful abnormality on bread swallows.

**Results:** 72 patients referred with dysphagia and diagnosed with normal HRM were selected. In the asymptomatic group, 7/22 patients showed abnormality on bread swallows. In the symptomatic group, 45/50 showed abnormal motility. (P = 0.0001) ROC analysis showed that having > 33.3% abnormal bread swallows has sensitivity of 72%, specificity of 90.91% and likelihood ratio of 7.9 to detect patients who may have abnormal motility and dysphagia on bread swallows.

Analysis of water swallow parameters comparing the asymptomatic group against the symptomatic group with abnormal motility on bread swallows did not reveal any significant difference in HODQ score (P = 0.2), IRP (P = 0.17), DL (P = 0.3) and peristaltic abnormalities (P = 0.4).

**Conclusion:** Performing solid swallows on HRM can explain dysphagia in a considerable number of patients with dysphagia and normal routine HRM. This complementary test is readily available, and avoids the need for Barium swallowing and radiation exposure.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1525 PER ORAL ENDOSCOPIC MYOTOMY: A PROSPECTIVE EVALUATION OF 136 CONSECUTIVE PATIENTS WITH ESOPHAGEAL ACHALASIA

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**Introduction:** Peroral endoscopic myotomy (POEM) is becoming a standard endoscopic procedure for esophageal achalasia. Nevertheless, mid- and long-term data should confirm favorable short-term outcomes of POEM. In this prospective, single-center study we report mid-term results of POEM.

**Aims & Methods:** Since 2012, a total of 139 POEM procedures have been performed in 136 patients with achalasia (61 women, 75 men, mean age 47). A follow up at 3, 6, 12, 24 and 36 months was completed in 109, 90, 76, 38 and 5 patients. The primary outcome was treatment success defined as an Eckardt score < 3 at 12 and 24 months (data at 36 months has not been analyzed due to a low number of patients who completed 36 M follow-up). Three months after POEM, endoscopy, high-resolution manometry and 24-hours pH metry monitoring were performed.

**Results:** A. PROCEDURE: POEM was successfully completed in most of the patients, two procedures failed due to submucosal fibrosis, one of these patients underwent successful re-POEM. The median length of the procedure was 67.5 minutes (range 28–185). The median myotomy length was 13 cm (6–19). In 71 patients (52.2%) capnoperitoneum had to be decompressed, and 66 patients (48.5%) experienced a subcutaneous emphysema which resolved spontaneously. Only one serious postoperative complication occurred and required prolonged hospitalization with thoracic drainage due to a pleural effusion. All remaining patients were dismissed on post-operative day 1 or 2. We observed the following minor complications: inadvertent mucosotomy 11x (7.9%); respiratory instability during POEM 2x (1.4%); bleeding at the entry site 4x

**Abstract No:P1527**

**Table 1:** Densities of (cells/mm$^2$) duodenal enteroendocrine cells of control subjects and of PI-IBS and idiopathic IBS patients before and after receiving FMT.

| Hormone | Control | PI-IBS, before | PI-IBS, after | Idiopathic IBS, before | Idiopathic IBS, after | *P-value | **P-value |
|---|---|---|---|---|---|---|---|
| **Chromogranin A** | 236 ± 32 | 385 ± 28 | 463 ± 17 | 399 ± 33 | 323 ± 11 | 0.009[b] | 0.066 |
| **Serotonin** | 76 ± 12 | 110 ± 6 | 180 ± 14 | 159 ± 27 | 101 ± 16 | 0.037[a] | 0.046[a] |
| **Somatostatin** | 43 ± 5 | 55 ± 3.4 | 85 ± 3.9 | 57 ± 7.8 | 47 ± 5.2 | 0.0008[c] | 0.047[a] |
| **Cholecystokinin** | 81 ± 4 | 128 ± 6 | 139 ± 8 | 128 ± 9 | 90 ± 12 | 0.2 | 0.015[a] |
| **Secretin** | 77 ± 4 | 83 ± 13 | 92 ± 17 | 91 ± 6 | 81 ± 3 | 0.3 | 0.1 |
| **Gastric inhibitory peptide** | 54 ± 5 | 65 ± 4 | 92 ± 5 | 70 ± 9 | 65 ± 8 | 0.04[a] | 0.6 |

Data are presented as the mean ± SEM. a: $P < 0.05$, b: $P < 0.01$, c: $P < 0.0001$; *PI-IBS patients before vs. after FMT, ** Idiopathic IBS patients before vs. after FMT.

(2.8%); difficult entry site closure 2x (1.4%) and large subcutaneous emphysema 2x (1.4%). B. TREATMENT RESULTS: 3, 6, 12, and 24 months after POEM, treatment success was achieved in 105, 87, 75 and 33 patients 96% (95% CI: 93–100), 97% (92–100), 99% (94–100), and 87% (71–98). At 24 months, 5 patients (13.2%) experienced a disease recurrence; a majority of these patients (3 pts.) underwent the procedure among the first 20 operated patients. The median Eckardt score decreased from 7 to 0 at 3, 6, 12 months, and to 1 at 24 months; $p < 0.001$. Quality of life significantly improved, median Eyspach-Williams score was 105 (27–133) before POEM vs. 131 (70–144), 138 (98–144), 139 (107–144) and 140 (99–144) at 3, 6, 12 and 24 months after POEM, $p < 0.001$). Heartburn was present in 25 patients (22.9%), 19 (25%) and 13 (34.2%) at 3, 12 and 24 months and a total of 35 patients (33%) have been treated with proton pump inhibitors. A mild reflux esophagitis was diagnosed in 36 patients (33%) and a pathological gastro-esophageal reflux (DeMeester score $>14$) was detected in 35 (32%) patients.

**Conclusion:** POEM is a safe and effective treatment modality in patients with achalasia with excellent short term results. However, the 24 months recurrence rate was 18.4% which might be partially explained in consequence of a learning curve. Mild reflux esophagitis and pathological gastroesophageal reflux are present in more than one third of patients and regular treatment with a PPI should be considered in all patients after POEM.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1526 WHATS'S THE IMPACT OF CONTINUNG MEDICAL EDUCATION ON THE INCIDENCE OF ACHALASIA?

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**Introduction:** Achalasia is a rare esophageal motility disorder most probably underestimated. Few epidemiological studies around the world have been devoted to it.

**Aims & Methods:** to investigate the epidemiology of achalasia in our country and to determine the impact of continuing medical education on incidence of achalasia. This study was carried out in two steps (1990–1998 and 1999–2014) at our institution which is the national reference center in the management of the esophageal motility disorders. During the second step we conducted a campaign of Continuing Medical Education (CME), on diagnosis and therapeutic aspects of the disease, including its 48 provinces. Annual incidence and prevalence were calculated by relating the number of diagnosed cases to 100.000 inhabitants and we compared the incidence between the two periods. Each underwent barium swallow, upper endoscopy and esophageal manometry.

**Results:** From 1990 to 2014, 1256 patients were diagnosed with achalasia. Overall prevalence was 3.14/100.000 inhabitants (95% CI; 2.97–3.31). The mean annual incidence raised from 0.04 (95% IC; 0.028–0.052) during the 1990s to 0.27/100.000 (IC; 0.215–0.321) during the 2000s. The incidence of the disease was two and half times higher in the north and the center compared to the south of the country. Among 1256 patients, 129 (10%) were children and 97 (7.7%) had an Allgrove syndrome. Familial achalasia was noticed in 18 different families. Patients had dysphagia (99%), Regurgitation (83%), Chest pain (51%), heartburn 24.5% and weight loss (70%). The lower esophageal sphincter was hypertensive in 53% and hypotensive in 0.6%.

**Conclusion:** the mean incidence of achalasia in our country is at least 0.27/100.000 inhabitants. This study showed a good impact of CME on incidence of achalasia. The variability between different regions of the country is probably related to genetic and environmental factors.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1527 EFFECT OF FAECAL MICROBIOTA TRANSPLANTATION ON THE SYMPTOMS AND DUODENAL ENTEROENDOCRINE CELLS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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**Introduction:** Irritable bowel syndrome (IBS) is caused by several factors including altered gut microbiota and altered neuroendocrine system. The main trigger of the enteroendocrine cells is the luminal content of the gut. The densities of the gut enteroendocrine cells are abnormal in IBS patients (1). Faecal microbiota transplantation (FMT) has improved the symptoms of IBS patients (2). In a 5 year-follow-up after the Giardia outbreak in the year 2004 in Bergen, Norway, more than 50% of the patients still had abdominal complaints and were diagnosed to have post-infectious IBS (PI-IBS).

**Aims & Methods:** The aim of the study was to investigate the effect of FMT on the symptoms and duodenal enteroendocrine cells in patients with diarrhoea predominant IBS (IBS-D). The study included 12 patients with IBS-D according to Rome III criteria (3 females and 6 males, age range 21–44 years) and three patients were excluded. The patients were divided according to the cause of IBS into PI-IBS ($n = 4$) and idiopathic IBS ($n = 5$). All the patients received FMT, freshly donated from their relatives. The patients completed the following questionnaires before and 3 weeks after FMT: IBS symptom questionnaire, IBS-symptom severity scoring system (IBS-SSS), Bristol stool form scale, the Eysenck personality questionnaire (EPQN-12) and Hospital anxiety and depression (HAD). The patients underwent gastroscopies with biopsies taken from the descending part of the duodenum at baseline and 3 weeks after FMT. The biopsies were immunostained for all enteroendocrine cell types using ultraView Universal DAB Detection Kit and quantified using computerized image analysis. Duodenal biopsies from a group of 14 control subjects (9 females and 5 males, age range 26–70 years) previously immunostained and quantified (using the same techniques) for all enteroendocrine cell types were borrowed from another research project that belongs to our group (3).

**Results:** The scores of IBS symptoms were significantly reduced 3 weeks after receiving FMT; total ($P = 0.0001$), nausea ($P = 0.004$), bloating ($P = 0.0003$), abdominal pain ($P = 0.005$), constipation ($P = 0.02$), diarrhoea ($P = 0.0002$) and anorexia ($P = 0.096$). The total scores of IBS-SSS and Bristol stool form scale, but not EPQN-12 and HAD, were significantly reduced 3 weeks after receiving FMT ($P = 0.0002$, 0.02, 0.18 and 0.08, respectively). The densities of the duodenal enteroendocrine cells before and 3 weeks after receiving FMT are presented in Table 1.

**Conclusion:** This is the first study where the interaction between the gut microbiota and the enteroendocrine cells is reflected by a change in the densities of the duodenal enteroendocrine cells in IBS patients following FMT. The positive effects of FMT may be attributed to the crosstalk between the gut microbiota and the enteroendocrine cells and contributed to the improvement in symptoms of IBS.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1528 FUNCTIONAL HEARTBURN: A PILOT RANDOMIZED TRIAL COMPARING CITALOPRAM VS. AMITRIPTYLINE AND NO TREATMENT

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**Introduction:** Functional heartburn (FH) is diagnosed in patients with negative endoscopy and pH monitoring who have resistant reflux symptoms after therapy with proton pump inhibitors (PPI) (Rome III). Antidepressants are frequently prescribed to treat FH, even though there is little evidence of their efficacy in such patients.
**Aims & Methods:** We performed a randomized trial to evaluate the efficacy of citalopram or amitriptyline versus no treatment on symptoms of patients with FH. Patients with normal endoscopy and typical reflux symptoms (heartburn, regurgitation), despite PPI twice daily, underwent ambulatory 24-hour pH monitoring. Distal esophageal acid exposure (% time pH $< 4$) and symptom index (SI) were measured. Patients with a normal distal esophageal acid exposure time and a negative SI were classified as having FH. Thereafter, they were randomly assigned to one of three treatment groups for 3 months: citalopram 20 mg, amitriptyline 50 mg, or observation. The end point was complete disappearance of reflux symptoms at the end of treatment.
**Results:** Over a two-year period, 43 patients (27 females; mean age $55 \pm 17$ years) were diagnosed with FH and were randomized to receive once daily citalopram ($n = 14$), amitriptyline ($n = 14$) or no treatment ($n = 15$). After 3-months follow-up, disappearance of reflux symptoms was reported by 5 (35.7%) patients treated with citalopram, 6 (42.8%) patients treated with amitriptyline, and 1 (6.7%) patient without treatment ($p = 0.033$ for no treatment vs. citalopram/and amitryptiline therapy).
**Conclusion:** Both citalopram and amitryptiline are effective pharmacological options in the symptomatic relief of patients with well characterized FH.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1529 BELCHING AND TRANSIT OF GASTRIC GAS IN HEALTHY HUMANS

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**Introduction:** During meals, a wide range of gas volumes enters into the stomach. Ingested gas is mainly nitrogen, a poorly absorbed gas that needs active transport and evacuation to be eliminated from the gut. Evacuation of gastric gas can be achieved by 2 ways: gas emptying to the small intestine, or triggering of the belching reflex by gastric distension. However, the normal ways of transit and evacuation of free gastric gas have been poorly investigated.
**Aims & Methods:** Our aim was to study the dynamics of free gastric gas in healthy subjects, and the correlation between gas retention, rectal and oral gas evacuation. In 24 healthy volunteers without gastrointestinal symptoms (14 women and 10 men, age-range 21–33 yrs), 1500 ml of a mixture of non-absorbable gases was infused into the stomach, 5-cm caudal to the lower margin of the LES. In groups of 6 volunteers the following gas infusion rates were tested: 0 ml/min (sham infusion), 25 ml/min, 50 ml/min and 100 ml/min. In the subjects receiving sham infusion, 400 ml/min of gas were infused at the end of the study until belching occurred. Belching, by an esophageal multilumen impedance manometry catheter, and rectal gas evacuation, via a rectal tube connected to a barostat, were continuously recorded for 90 min.
**Results:** Sham infusion was associated to small rectal gas evacuation ($187 \pm 94$ ml after 90 min), and virtually no belching ($0 \pm 0$ belches). In contrast, gastric gas infusion induced a significant increment in rectal gas evacuation ($1129 \pm 281$ ml, $1362 \pm 410$ ml, and $1116 \pm 281$ ml of gas after infusion at 25, 50 and 100 ml/min, respectively; $p < 0.05$ vs sham infusion for all), and a minor increment of the recorded belching ($3 \pm 2$; $4 \pm 2$ and $4 \pm 2$ belches at 25, 50 and 100 ml/min, respectively; $p = 0.451$ vs sham) that were similar at all infusion rates. Infusion of gas at 400 ml/min induced belching in all subjects at a lower infused volume ($703 \pm 132$ ml) than the infused volume associated with first belching at the lower infusion rates ($1300 \pm 148$ ml, pooled data of infusion at 25–100 ml/min). Overall, there was a negative correlation between rectal gas evacuation and belching ($r = -0.66$; $p < 0.05$).
**Conclusion:** In healthy subjects, gastric gas is rapidly emptied to the small bowel and propelled to the rectum preventing gas retention and gastric distension. Only when gas arrives to the stomach at a very high rate the belching reflex, acting as a reserve defense mechanism, is activated and oral venting of gas occurs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1530 ROLE OF ACID REFLUX AND IMPACT OF HRM PARAMETERS IN PATIENTS WITH NON-OBSTRUCTIVE DYSPHAGIA

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**Introduction:** Non-obstructive dysphagia (NOD) is a real challenge in clinical practice. The role of gastro-esophageal reflux disease (GERD) in eliciting NOD is not yet fully elucidated. Moreover, it is still not clear how findings of high resolution manometry (HRM) may relate to esophageal bolus transit.
**Aims & Methods:** To assess the role of HRM findings, of GERD presence and of acid suppression in dysphagia perception. Method: 44 consecutive patients with recurrent dysphagia underwent combined HRM-impedance followed by 24 h impedance-pH. Dysphagia was scored on a 5-point Likert scale from 'occasionally' to 'always'. Patients performed upper endoscopy with biopsies within 3 months before to rule out hiatal hernia and/or eosinophilic esophagitis. HRM was performed in a semi-recumbent position with a catheter incorporating 36 solid state pressure sensors and 9 impedance segments. 10 saline (5 ml) swallows at 30-sec intervals were analyzed in each patient. Tracings were analyzed according to the Chicago classification v3.0. Bolus transit time (BTT) during HRM was the time between bolus entry in the proximal impedance segment to exit from the most distal segment. 44 GERD patients with typical symptoms, responding to PPIs, not complaining of dysphagia, underwent the same protocol. 18 NOD patients repeated the study while on PPIs (Esomeprazole 40 mg/o.i.d.), after a 4-week treatment.
**Results:** 4 NOD patients presenting evidence of outflow obstruction and 3 patients with achalasia were excluded. The remaining 37 NOD patients were considered for the analysis. 15/37 NOD patients (40%) and 19/44 (43%) GERD patients presented pathological acid exposure time (AET). HRM data are in Table 1. NOD AET+ patients showed a significantly lower mean DCI value than NOD AET-. Mean BTT values were similar in NOD and in GERD patients both with normal and abnormal AET. A significant correlation between DCI and BTT values was found only in NOD AET+ patients. 10/15 NOD AET+ and 8/22 NOD AET- patients repeated the protocol while on PPI. All these 18 NOD patients presented normal AET on treatment. Data are in Table 2. During PPI therapy, patients reported a dysphagia score significantly lower than off therapy. NOD AET+ patients, after 4 weeks of treatment, presented a significantly higher mean DCI value.

**Table 1**

| | NOD AET+ | NOD AET- | GERD AET+ | GERD AET- |
|---|---|---|---|---|
| IRP 4 sec (mmHg) | $8.3 \pm 1.4$ | $8.9 \pm 1.3$ | $7.9 \pm 2.1$ | $8.4 \pm 2.1$ |
| DL (sec) | $4.8 \pm 1.1$ | $4.9 \pm 1.1$ | $5.2 \pm 1.1$ | $5.2 \pm 1.1$ |
| DCI (mmHg-s-cm) | $669 \pm 298$* | $1438 \pm 597$ | $947 \pm 257$ | $1289 \pm 257$ |
| BTT (sec) | $13.8 \pm 4.6$ | $13.1 \pm 1.9$ | $13.4 \pm 3.1$ | $12.4 \pm 1.6$ |
| DCI-BTT correlation (Spearman Rho) | -0.71 (p 0.0027) | -0.39 (p 0.072) | -0.31 (p 0.09) | -0.33 (p 0.13) |

*$p < 0.01$ vs NOD AET-

**Table 2**

| | NOD AET+ | NOD AET+ on PPI | NOD AET- | NOD AET- on PPI |
|---|---|---|---|---|
| Dysphagia score | 4.1* | 1.4 | 3.2** | 1.8 |
| DCI (mmHg-s-cm) | $701 \pm 281$§ | $1038 \pm 327$ | $1047 \pm 127$ | $1122 \pm 111$ |
| BTT (sec) | $14.1 \pm 4.5$ | $13.2 \pm 1.7$ | $13.2 \pm 3.2$ | $12.5 \pm 1.5$ |

*$p < 0.01$ vs NOD AET+ on PPI ** $p < 0.05$ vs NOD AET- on PPI §$p < 0.05$ vs NOD AET+ on PPI

**Conclusion:** 40% of NOD patients showed a pathological AET and a lower esophageal contractile vigor. In NOD AET+ patients DCI correlates with BTT. Reduced dysphagia perception following acid suppression together with a significant increase of DCI, in a subgroup of NOD, strongly suggest that increased AET may enhance the perception of bolus impaction by sensitizing esophageal mucosa to its transit.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1531 SUPRAGASTRIC BELCHING (SGB) AND GASTRO-OESOPHAGEAL REFLUX: CAUSE AND EFFECT?

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**Introduction:** Supragastric belching (SGB) is characterised by rapid antegrade and retrograde flow of air in the oesophagus that does not reach the stomach*. Whilst proactive SGB is a behavioural phenomenon, reactive SGB occurs in

response to a particular stimulus. Currently treatment for SGB is behavioural therapy however this may not be the most appropriate treatment for patients with reactive SGB. We aimed to ascertain prevalence of proactive versus reactive SGB in response to a certain pathological stimulus i.e. GOR.
**Aims & Methods:** The database of the Oesophageal Physiology Laboratory at Guy's Hospital London were retrospectively searched (November 2014 – present) for patients diagnosed with SGB (>13 SGBs within 24 hrs). The 24-hour pH-impedance studies were analysed to differentiate proactive SGB from reactive (proactive SGB being an SGB without preceding reflux event (or preceding event lasting < 1 second), and reactive SGB being an SGB with preceding reflux event (> 1 second)). A patient was then labelled as having predominantly reactive SGB (PR-SGB) if >60% of their SGB was reactive and having predominantly proactive SGB (PP-SGB) if >60% of their SGB was proactive. Reflux Diseases Questionnaire (RDQ) score was obtained for all patients. P value <0.05 was considered significant.
**Results:** 28 patients identified for this study (14 males (M), 14 females (F), mean age 51 [27–75]). 82% of patients had PP-SGB events, 11% PR-SGB and 7% had the same number of proactive and reactive SGB. The most common symptoms in patients with PR-SGB were: heartburn 66.6%, belching 66.6% and throat burning sensation 66.6% and, in patients with PP- SGB: belching 68%, heartburn 39% and regurgitation 21%. In total, in all 28 patients, proactive SGBs accounted for 1124 and reactive 216 of SGB events (19.22% of all SGBs being reactive). The 3 patients with PR- SGB had an average RDQ of 3.53, whilst the average RDQ for the patients with PP- SGB was significantly lower 2.36 ($p = 0.00004$). There was 1 patient with 100% proactive SGB and no patient with purely reactive SGB. The median presentation of reactive SGB was 15.38%.
**Conclusion:** Treating GORD may resolve SGB in a small group of patients and ameliorate potential psychological stress caused by a behavioural therapy referral. Whether the remaining SGB events are purely behavioural or in reaction to other types of stimuli other than GOR requires further investigation. Having a high RDQ score may help in identifying patients with PR-SGB.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1532 PROKINETICS FOR THE TREATMENT OF FUNCTIONAL DYSPEPSIA: A BAYESIAN NETWORK META-ANALYSIS

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**Introduction:** Controversies persist regarding the effect of prokinetics for the treatment of functional dyspepsia (FD). The aim of this study was to assess the efficacy of prokinetics agents for the treatment of functional dyspepsia.
**Aims & Methods:** Randomized controlled trials (RCTs) of prokinetics for the treatment of FD were identified from core databases. Symptom response rates were extracted and analyzed using odds rations (ORs). A Bayesian network meta-analysis was performed using the Markov chain Monte Carlo method in WinBUGS and NetMetaXL.
**Results:** In total, 26 RCTs, which included 6789 patients with FD who treated 6 different prokinetics or placebo were identified and analyzed. Metoclopramide showed the best SURCA probability (92.3%), and better efficacy than those of itopride (OR: 2.79, 95% credible regions: 1.29–6.21), and acotiamide (OR: 3.07, 95% credible regions: 1.43–6.75), followed by trimebutine (SUCRA probability 75.9%), and mosapride (SUCRA probability 62.9%). Domperidone (SUCRA probability 62.6%) also showed better efficacy than those of itopride (OR: 1.37, 95% credible regions: 1.07–1.77), and acotiamide (OR: 1.51, 95% credible regions: 1.04–2.18).
**Conclusion:** In this analysis, metoclopramide showed best efficacy for the treatment of FD. Considering the adverse events related to metoclopramide or domperidone, short-term use of these agents or alternative use of trimebutine or mosapride could be recommended for the symptomatic relief of FD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1533 PREDICTION OF COMPLICATIONS AFTER PERORAL ENDOSCOPIC MYOTOMY

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**Introduction:** Achalasia is a functional motility disorder of the esophagus. Peroral endoscopic myotomy (POEM) is a revolutionary therapy for achalasia that was first reported by Inoue and colleagues. (1) POEM has been performed worldwide, safely and with positive outcomes. However, complications associated with POEM are rarely reported. The objective of this study was to conduct a detailed review of the complications occurring after POEM and the predictive factors of these complications.
**Aims & Methods:** Between September 2011 and September 2015, 142 patients underwent POEM at our institution. Complications were graded according to the Clavien-Dindo classification system. The patients were classified into two groups as follows: (A) those without complications and (B) those with complications. Age, previous treatment of achalasia, preoperative comorbidities, symptom duration, type of achalasia (non-sigmoid vs. sigmoid), pre- and post-POEM Eckardt score, manometric findings, and treatment outcomes, including hospitalization duration and occurrence of complications, were compared between the groups by using chi-square and Student t tests.
**Results:** Of the 142 patients who underwent POEM, 17 (12.0%) experienced minor complications of grade £2. No other severe complications were observed in all the patients. Group A consisted of 125 patients; and group B, 17 patients. Operation time was significantly longer for group B than for group A (mean ± SD [range]: 205.9 ± 68.5 min [140–370 min] vs. 147.7 ± 44.9 min [75–345 min]; $p = 0.022$). Hospitalization duration was significantly longer for group B than for group A (mean ± SD [range]: 13.2 ± 10.7 days [10–50 days] vs. 7.1 ± 2.0 days [3–21 days]; $p < 0.001$. No statistically significant differences in age, previous treatment of achalasia, preoperative comorbidities, symptom duration, type of achalasia, Eckardt score, manometric findings, or mean duration of the myotomy procedure were found between the two groups. Significant decreases in Eckardt score and integrated relaxation pressure were achieved in both groups.
**Conclusion:** Minor complications occurred in only 12.0% of our patients, who were treated conservatively. No other severe complications were observed. POEM was safe and effective regardless of previous treatment of achalasia, symptom duration, type of achalasia, and manometric findings. Longer operating time was a predictive factor of complications occurring after POEM. In cases that need longer operating time, more attention is required in examinations after POEM.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1534 RETROSPECTIVE CASE SERIES OF GERD AFTER POEM: A COMPARISON OF ANTERIOR AND POSTERIOR MYOTOMY

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**Introduction:** Peroral endoscopic myotomy (POEM), a revolutionary form of endoscopic treatment for esophageal achalasia, is currently the standard of therapy for this condition. However, few studies have investigated the incidence and management of gastroesophageal reflux disease (GERD) associated with the direction of the myotomy. In the present study, we gathered retrospective data from our hospital and compared the incidence and management of GERD when the myotomy was made in the anterior or posterior wall, which are the two main surgical approaches.
**Aims & Methods:** We included 152 patients who underwent POEM at our hospital between September 2011 and January 2016. Patients who could not undergo the postoperative examination after three months or who were being continuously treated with oral proton pump inhibitors (PPIs) for conditions other than esophageal achalasia were excluded.
**Results:** The myotomy was made in the anterior wall in 93 patients (group A) and in the posterior wall in 54 patients (group P). After three months, we interviewed the patients, performed endoscopic tests, conducted a 24-h pH test, and investigated GERD after POEM. We found no statistically significant differences between patients in groups A and P in terms of age, sex, type of achalasia, and body mass index. There was a statistically significant improvement in the Eckardt score in patients in both groups after the procedure. The incidence of erosive esophagitis measured using the Los Angeles classification [LA-(grade)] in patients in group A was LA-N 31%, LA-A 46%, LA-B 12%, LA-C 11%, and LA-D 0%. The corresponding rates in patients in group P were LA-N 18%,

LA-A 32%, LA-B 25%, LA-C 25%, and LA-D 0%. The amount of time with pH of <4 as a proportion of monitoring time was 7% and 24% in patients in groups A and P, respectively. This statistically significant difference indicated a higher rate of GERD in patients who received a posterior wall myotomy. Symptomatic GERD occurred in 12% and 14% of patients in groups A and P, respectively. There were no patients with GERD who were difficult to clinically manage through the use of oral PPIs.
**Conclusion:** In the present study, postoperative GERD was more common in patients in posterior myotomy, while GERD can be managed with the use of oral PPIs. If the same trend in the post-POEM incidence of GERD is seen in future studies, patients should be notified during the informed consent process that the need for ongoing oral PPI therapy will be more likely after POEM if a posterior wall myotomy is made.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1535 PROTON PUMP INHIBITOR THERAPY IMPROVES NASAL SYMPTOMS AND INFLAMMATION IN PATIENTS WITH NONALLERGIC RHINITIS WITH NEUTROPHILS AND GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** The role of Gastroesophageal Reflux Disease (GERD) in causing extra-esophageal symptoms, is increasingly recognized with renewed interest. Nonallergic rhinitis (NAR) is defined as a compound of nasal symptoms in the absence of an allergic etiology and it is frequently observed in the clinical practice. Nasal cytology allows to identify the different NAR sub-types on the basis of the particular inflammatory cell infiltrate. Nonallergic rhinitis with neutrophils (NARNE) subtype pathogenesis highlights a chronic progressive inflammation process. To date, data about the etiopathogenetic role of the reflux in rhinitis and in particular in the form of NARNE are lacking.
**Aims & Methods:** To evaluate the effect of Proton Pump Inhibitor (PPI) therapy on the patients affected from both NARNE and GERD. Thirty-five patients referred to our ENT unit for nasal symptoms such as rhinorrhea, sneezing, and postnasal drip were enrolled. Visual analogue scale (VAS) for nasal symptoms, rhinomanometry, skin prick test and nasal cytology were performed. Exclusion criteria were infectious rhinosinusitis, ambient irritant exposure and/or a positive skin prick test. Of the 35 subjects with NAR, 20 (13F/7M, median age 48 years) showed the presence of neutrophils (neutrophils > 50% with absent spores and bacteria) at nasal cytology (NARNE) and were selected to perform a 24 hour pH-Impedance. Patients with a 24 hour pH-Impedance positive for GERD were treated with a high dose of oral PPI (40 mg x 2/day) for 8 weeks. A second pH-Impedance was performed during therapy whereas ENT examination and nasal cytology were performed at the end of treatment.
**Results:** Of the 20 patients with NARNE, 14 (70%) resulted to have pathological basal pH-Impedance values and 6 (30%) resulted to have normal basal values. PH-Impedance performed during PPI treatment showed the normalization of the number of refluxes (< 48) and pH values (< 4.2) in 9 (64.3%) out of the 14 patients with positive pH-Impedance at enrollment. PH-Impedance during treatment continued to be pathological in 3 (21.4%) patients with a pathological number of refluxes (2 with acid pH, 1 with normal pH values). Seven (77.8%) out of 9 patients with normal pH-Impedance values under treatment showed the simultaneous normalization of nasal cytology and symptom improvement whereas two (22.2%) subjects did not show any significant clinical and nasal cytology improvement. Two (14.3%) subjects experienced improvement in symptoms and showed the normalization of nasal cytology but refused to repeat the pH-Impedance during therapy.
**Conclusion:** Treatment with high dose of oral PPI for 8 weeks seemed to be effective in improving symptoms and in reducing nasal inflammation in a significant number of patients with NARNE and GERD diagnosis by pH-Impedance.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1536 LONG TERM CAPSAICIN INGESTION REDUCES SYMPTOMS IN PATIENTS WITH CHEMOSENSITIVE FUNCTIONAL DYSPEPSIA

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**Introduction:** Capsaicin ingestion induces abnormal upper GI sensations in half of patients with functional dyspepsia, as can be demonstrated by the oral capsaicin capsule test (Hammer et al, *NGM* 2008, Führer et al, *NGM* 2011). Sensations induced by gastric capsaicin are distinct from sensations induced by stimulation of mechanoreceptors (Hammer & Vogelsang, *NGM* 2007). Repeated capsaicin intake can improve upper gastrointestinal complaints in patients with functional dyspepsia (Bortolotti et al, *APT* 2002). Long term capsaicin consumption affects chemo- and mechanoreceptors differently (Führer & Hammer, *NGM* 2009).
**Aims & Methods:** The aims of the present study was to investigate whether the ingestion of capsaicin over a four week period can improve symptoms of functional dyspepsia (FD) and if chemosensitive or rather non-chemosensitive patients benefit more from oral capsaicin intake. To determine their chemosensitivity n = 59 patients with FD received the oral capsaicin capsule test (0.75 mg capsaicin capsules, ingested in the fasting state). After a one week run-in period patients received capsaicin capsules (0.25 mg; tid) for four weeks and a standard numeric rating scale was filled out daily to determine the type and severity of symptoms. For each week the sum of each individual symptom score as well as an overall score was calculated. Results are given as mean±SEM, $p < 0.05$ was considered significant.
**Results:** 32 patients (54%) had a positive capsaicin test, thus were considered chemosensitive (caps pos), 27 (46%) were non-chemosensitive (caps neg). 14 patients did not finish the 4 week study (10 caps pos, 4 caps neg, $p < 0.05$), mainly because of pain in the first two study weeks. 45 patients finished the study (22 caps pos; 23 caps neg). Overall symptoms in the run-in period were comparable in the caps pos ($9.4 \pm 4.1$) and caps neg group ($7.1 \pm 3.3$) (NS). At the end of the 4 week treatment period symptoms were significantly reduced as compared to the run-in period in the caps pos group ($5.7 \pm 4.9$; $p < 0.05$), but not in the caps neg group (NS). Significant improvement of epigastric pain ($p < 0.01$), postprandial fullness ($p < 0.01$) and early satiation ($p < 0.05$) started at week 3, while epigastric burning did not significantly change (NS).
**Conclusion:** Chemosensitive FD patients may benefit from a 4 week trial of oral capsaicin, especially by improved epigastric pain, postprandial fullness and early satiety. However, a high dropout rate was observed, mainly due to pain developing in the early phase of treatment in the chemosensitive group. Considering capsaicin sensitivity as the entry criterion in this group, symptoms that develop after capsaicin ingestion is not surprising after all.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1537 THE OUTCOMES AND QUALITY OF LIFE OF CHINESE PATIENTS WITH ACHALASIA AFTER PERORAL ENDOSCOPIC MYOTOMY: A MULTI-CENTER CLINICAL STUDY

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**Introduction:** To assess quality of life (QOL) and psychological state of patients with achalasia after peroral endoscopic myotomy (POEM).
**Aims & Methods:** Six hundred and eight-seven achalasia patients underwent POEM from Jan 2011 to December 2015. The data on clinical evaluation and QOL before therapy, at 1 month and 6 months postoperation were collected and analyzed. Meanwhile, Zung's Self-rating anxiety Scale (SAS) and self-rating depression scale (SDS) were used to assess the anxiety and depression.
**Results:** All the six hundred and eighty-seven patients underwent POEM successfully. By comparing the data of the preoperative with that of 1 month and 6 months after POEM respectively, we found that: mean Eckardt score decreased ($8.1 \pm 1.3$ vs $1.27 \pm 0.31$, $8.1 \pm 1.3$ vs $0.61 \pm 0.52$, all $p < 0.05$), esophagus diameter reduced (53.82 mm vs 32.1 mm, 53.82 mm vs 28.31 mm, all $p < 0.05$), and esophageal manometry declined (31.7 mmHg vs 12.3 mmHg, 31.7 mmHg vs 10.1 mmHg, all $p < 0.05$). No complications and recurrence occurred in all cases. At each time point, postoperative QOL scores were higher than those

of preoperative ($p < 0.05$). The anxiety and depression scores of preoperative patients were higher than normal group (SAS $51.32 \pm 7.26$ vs. $31.72 \pm 7.21$, SDS $53.17 \pm 5.98$ vs. $29.75 \pm 8.01$, all $p < 0.05$), which were closely related to the severity degree of symptom ($p < 0.05$). A comparison between the postoperative and preoperative groups (SAS $51.32 \pm 7.26$ vs. $37.2 \pm 7.18$, SDS $53.17 \pm 5.98$ vs. $35.72 \pm 7.36$, all $p < 0.05$) demonstrated a significent difference reduced by POEM.

**Conclusion:** POEM is safe and effective for treating achalasia, it can relieve clinic symptoms as well as improve patients' QOL, effectively relieving negative emotion.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1538 FUNCTIONAL DYSPEPSIA AND BINGE EATING DISORDERS IN ITALIAN MORBIDLY OBESE PATIENTS


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**Introduction:** Binge Eating Disorder (BED) occurs in a subset ranging from 27 to 47% in severely obese persons undergoing bariatric surgery. BE disorders have been already associated with the experience of both upper and lower gastrointestinal (GI) symptoms.

**Aims & Methods:** We aimed to investigate the prevalence of Functional Dyspepsia (FD) and its two subgroups: the Postprandial Distress Syndrome (PDS) and the Epigastric Pain Syndrome (EPS) in a morbidly obese southern Italy adult population; to evaluate the association between FD and the presence of BED.

Methods. One hundred and forty-three consecutive morbidly obese patients were recruited from an outpatient clinic devoted to the surgical therapy of obesity and related disorders. All participants were questioned and scored for the presence or the frequency-intensity of 4 cardinal symptoms of FD according to Rome III criteria: early satiation, epigastric fullness, epigastric pain and burning. A psychologist performed a structured interview for psychological assessment and administered the Italian version of the Binge Eating Scale (BES).

**Results:** FD was found in 17/143 obese patients. 5/17 (29.4%) of obese patients with BED and 12/126 (9.5%) of obese patients without BED ($p = 0.003$). There was a significant association between obese patients with BED and PDS, while only one obese patients with BED fulfilled the diagnostic criteria for EPS ($p = 0.01$). Obese patients with BED showed significantly higher frequency-intensity scores for epigastric fullness ($1.90 \pm 1.91$vs $0.37 \pm 0.97$, $p = 0.003$) compared to obese patients without BED. No patients in both groups reported early satiation, and no difference in the frequency-intensity score of epigastric pain and burning was found between groups ($p = 0.79$ and $p = 0.21$, respectively).

**Conclusion:** Obese patients with a BED showed a significantly higher prevalence of Postprandial Distress Syndrome. Probably, the excessive intake of food over short time could overcome the functional accommodation and emptying, contributing to the genesis of GI symptoms. A greater knowledge of the pathophysiological mechanisms underlying these symptoms could be important in the clinical management of this emerging class of patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1539 METAANALYSIS OF CLINICAL TRIALS ON STW 5


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**Introduction:** Since the prokinetics, which had been introduced to the therapy of functional gastrointestinal diseases in the 70 s and 80 s, are not longer available due to restrictions of their marketing authorizations based on rare but severe side effects, well-proven therapeutic options gain increased attention. One of these is STW 5 (Iberogast), for which more than 5 decades of therapeutic experience in more than 60 Mio patients are available.

**Aims & Methods:** Whether also the available clinical data comply to modern standards for a proof of efficacy was now tested by a meta-analysis including the randomized placebo-controlled double blind trials available in the therapeutic indication functional dyspepsia. The original data from the trials were entered and evaluated regarding demografic data and primary endpoints (ANCOVA).

**Results:** The primary outcome variable, the validated gastrointestinal symptom score (GIS) [1], as well as the therapeutic dose (3 x 20 drops/day) were identical in all trials, so allowing a uniform evaluation. The full analysis set (FAS) included 557 patients (272 resp. 285 for placebo resp. verum). The mean age (48 resp. 49 years), the mean body size (in both groups 168.7 cm), the mean body weight (72.0 resp. 72.2 kg), the BMI (25.35 resp. 25.54), the gender disitribution (67.3 resp. 69.5% females), the duration of the disease at the time of inclusion and the baseline of the GIS (11.6 resp. 11.5 points) were very well comparable between both groups. For the primary variable GIS the difference between placebo and verum after 28 days of treatment showed a highly significant ($p < 0.0001$) difference between placebo and verum (6.7 resp. 4.7 points).

**Conclusion:** This meta analysis therefore clearly shows the efficacy of STW 5 (Iberogast) according to present standards and in addition the high quality of the trials, which is indicated e.g. by the very good balance between both patient groups. Additional insights can be expected from additional analyses, as e.g. the evaluation of different subgroups with specific predominant symptoms or demographic properties.

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## P1540 IMPACT OF CONCOMITANT DYSPEPSIA AND IRRITABLE BOWEL SYNDROME ON SYMPTOM BURDEN AND PSYCHOSOCIAL CHARACTERISTICS IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** Gastroesophageal reflux disease (GERD), dyspepsia and irritable bowel syndrome (IBS) are highly prevalent gastrointestinal disorders in the general population. They frequently overlap with each other and affect quality of life.
**Aims & Methods:** The aim of the study was to investigate the impact of overlap on GERD symptom burden. We also investigate whether GERD overlapping dyspepsia or/and IBS would have an impact on clinical and psychological features as compared with GERD alone. We performed a nested case-control study in a GERD cohort. 2752 subjects were initially screened from a health check-up population, and 273 subjects were enrolled for the final analysis. We compared the clinical and psychological factors between subjects with GERD alone and with overlap of two or all three diseases. All participants underwent an evaluation with questionnaires including Reflux Disease Questionnaire score, Pittsburgh Sleep Quality Index, Taiwanese Depression Questionnaire, and State-Trait Anxiety Inventory before receiving endoscopic exam. Dyspepsia and IBS are based on the Rome III diagnostic criteria. Metabolic syndrome was defined by the National Cholesterol Education Program Adult Treatment Panel III definition.
**Results:** Among the GERD population, 26 with IBS (GERD-I), 60 with dyspepsia (GERD-D), and 25 subjects with overlap of all three conditions (GERD-I + D). GERD-D and GERD-I + D subjects had more severe GERD symptoms as compared subjects with GERD alone ($P < 0.001$). Subjects with overlapping dyspepsia or/and IBS showed a significant increase in the severity of depression than subjects with GERD alone ($P < 0.001$). Notably, sleep quality and anxiety scores did not differ significantly between subjects with overlapping diseases and GERD alone.
**Conclusion:** Our study demonstrates that disease overlap in GERD population is associated with greater symptom burden and greater depression. We also highlight that clinical awareness of such overlapping diseases would improve the therapeutic strategy of GERD in clinical practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1541 A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF THE ADDITIVE EFFECT OF FAMOTIDINE ON ACOTIAMIDE TREATMENT FOR FUNCTIONAL DYSPEPSIA

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**Introduction:** Acotiamide, with gastroprokinetic activity, is used for treating functional dyspepsia (FD), and postprandial distress syndrome (PDS). For epigastric pain syndrome (EPS), acid-suppressive agents are recommended. Many FD patients have PDS and EPS symptoms, suggesting combination therapy with acotiamide and acid-suppressive agents may be more effective; however, a randomized placebo-controlled study is lacking. We conducted this study to investigate the effect of famotidine, an acid-suppressive agent, on acotiamide in FD treatment.
**Aims & Methods:** Fifty FD patients were randomized blindly to receive famotidine or placebo with acotiamide for four weeks. Efficacy was assessed by an overall treatment effect (OTE) every two weeks, based on weekly changes of individual total, PDS and EPS symptom scores, and epigastralgia-related, or epigastric fullness-related, impairment of quality of life (QOL).
**Results:** From the OTE assessment, patients who felt affected by treatment comprised 30.4% (39.1%) and 16.7% (45.8%) of famotidine and placebo groups, respectively, after two (four) weeks of treatment, with no significant difference between famotidine and placebo groups. Total individual symptom scores after four weeks' treatment were significantly decreased compared with pretreatment scores for famotidine and placebo groups. As for QOL impairment, a significant improvement was observed between pre- and post-treatments for famotidine and placebo groups, but was not observed between groups. Patients with markedly decreased ( > 50%) EPS symptom scores after two week treatments were significantly greater for the famotidine (57%) than the placebo (24%) group ($P = 0.004$).
**Conclusion:** Famotidine plus acotiamide may be effective in improving EPS symptoms at an early stage of treatment for FD patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1542 INCIDENCE OF REFLUX SYMPTOMS AND EROSIVE ESOPHIGITIS AFTER PERORAL ENDOSCOPIC MIOMOTOMY (POEM) FOR ACHALASIA: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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**Introduction:** POEM represents a less invasive alternative, as compared with conventional laparoscopic Heller myotomy, for achalasia patients. It cannot be excluded, however, that the apparently high efficacy of POEM may be hampered by an excessive incidence of post-POEM reflux disease
**Aims & Methods:** Relevant publications in which patients affected by achalasia underwent POEM treatment were identified by PubMed databases for the period 2010–2016. From each study, the outcomes considered were incidence of post-procedure reflux (according to two subcategories: reflux symptoms and endoscopic findings) at follow-up.Since primary studies considered different time ranges, we pre-defined to pool outcomes at early (<12 months) and late (>12 months)) follow-up. Data were analyzed using fixed-effect model and random-effect model. Heterogeneity was assessed using the $I_2$ test. Per-protocol analyses were reported.
**Results:** A total of 35 reports were included, accounting for a total of 2,208 cases with post-POEM follow-up with a median of 9 months(range 2–44). Regarding incidence of post-POEM reflux symptoms meta-analysis yields an overall pooled rate of 22.1% (95% CIs: 19.2–25.2] with significant heterogeneity($I^2$=54.5% $p < 0.001$). The short and long-term outcome was 20.8% [random-effect pooled estimate,95%CIs:17.0–25.2%] and 23.8% [random-effect pooled estimate,95% CIs: 20.2–26.2%] respectively. Significant intra-group heterogeneity was observed for short-time incidence ($I^2 = 59.6\%$;$p < 0.00$) while low heterogeneity was found for the long-term outcome($I^2 = 34.2\%$,$p = 0.1445$). However no inter-group heterogeneity was noted ($p = 0.313$),supporting the pooling of all studies into one pooled measure. According to meta-regression analysis, duration of follow-up(<12 months vs >12 months) was not associated with reflux symptoms ($p = 0.111$). However the geographical location where the study was performed (Europe/USA vs Asia) affected the overall outcome. The chance of being symptomatic over time was greater in studies performed in Europe/USA than that in studies performed in Asia (ORs, 1.66;95%CIs 1.26–2.18;$p < 0.001$). The Egger test was not significant for publication bias (regression coefficient, 0.40;$p = 0.561$). The overall pooled rate of all endoscopic findings at the follow-up was 36.6% [95% CIs:26.6–48.0%]. Differences between short term and long term outcome were not statistically significant($p = 0.837$). Although there was significant heterogeneity across the trials $I^2 = 85\%$;$p < .001$, a sensitivity analysis suggested that the data were not affected by the sequential exclusion of any particular trial from the pooled analysis. When restricting analysis to esophagitis of grade C or D, the overall post-procedure rate was 3.7% [95%CIs: 2.6–4.9%]. Low heterogeneity was found for this outcome [$I^2 = 31.3\%$[0%; 62.3%];$p = 0.11$]. The Egger test was not significant for publication bias [$p = 0.4217$]].
**Conclusion:** Incidence of reflux-related symptoms or endoscopic findings is quite frequent after POEM, occurring in 1 every 5 and 3 patients, respectively. However, occurrence of severe post-POEM esophagitis is quite rare, reassuring on the overall safety of the procedure.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1543 ESOPHAGEAL BASELINE IMPEDANCE AS A MARKER OF PATHOLOGICAL GASTROESOPHAGEAL REFLUX IN CHILDREN

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**Introduction:** It is believed that the low esophageal baseline impedance (BI) may reflect a compromised integrity of the esophageal mucosa and its increased sensitivity to hydrochloric acid.
**Aims & Methods:** The aim of the study was to analyze the esophageal baseline impedance and its correlation with the classical pH-metry parameters as a markers of pathological gastroesophageal reflux (GER) diagnosed based on the examination of 24-hour esophageal pH-impedance monitoring (MII-pH). Twenty-four-hour pH-impedance monitoring was performed in 77 children with suspected gastroesophageal reflux (42 boys, aged 5.4–17.9, average 11.4

years). Based on the results of the MII-pH study (the total duration of reflux episodes ≥ 1.4%) pathological GER was found in 24 children. Taking into account the pH-metry parameters GER patients were divided into two subgroups: group A - acidic GER (fT pH < 4 above 4.2%) (n = 14) and group B - weakly acidic GER (fT pH < 4 under 4.2%) (n = 10). The remaining patients – group C (n = 53) did not show the characteristics of patological GER. BI measurements were obtained in the distal esophagus in a continuous 6-hour period between 11:00 pm and 5:00 am during sleep. The results were compared between the groups and correlated with the classical pH-metry parameters (fT pH < 4 - total, upright and supine, the number of episodes > 5 min., duration of the longest episode and the total number of reflux episodes).
**Results:** The lowest esophageal baseline impedance has been shown in group A (median 1243 Ω), intermediate in group B (median 2184 Ω), the highest in group C (median 3081 Ω). Statistically significant differences of BI were found between groups ($X^2 = 14.97$, $p = 0.0006$), especially between groups A and C ($p = 0.000001$), and B and C ($p = 0.0079$). Regarding the whole studied group a statistically significant negative correlation were found between the BI and all analyzed pH-metry parameters ($r = -0.3$ up to $-0.55$; $p = 0.007$ up to $p = 0.0000$), whereas in the subgroups such relationship was only observed between the total number of reflux episodes in group B ($r = -0.75$; $p = 0.01$) and the fT pH < 4 above 4.2% in the supine position in group A ($r = -0.55$; $p = 0.03$).
**Conclusion:** Analysis of the esophageal baseline impedance may be an additional, useful parameter in the diagnosis of pathological gastroesophageal reflux in children.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1544 SPLITTING ESOPHAGO-GASTRIC JUNCTION MORPHOLOGY TYPE I: A BETTER PREDICTION OF GERD PATIENTS WITH A POSITIVE IMPEDANCE-PH MONITORING


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**Introduction:** High-resolution manometry (HRM) provides information on esophagogastric junction (EGJ) morphology, being able to distinguish whether the lower esophageal sphincter (LES) and crural diaphragm (CD) are superimposed or separated. Actually, three different subtypes can be described by means of HRM, and it was recently demonstrated that increasing separation between LES and CD could cause a gradual and significant increase of reflux. Type I morphology is the group with the lowest incidence of a positive impedance-pH test. However, this latter type also includes in its definition the presence of LES-CD axial separation up to 1 cm.
**Aims & Methods:** The aim of this study was to verify if splitting the EGJ Type I into two sub-types could better correlate with a positive impedance-pH test in patients with reflux symptoms. Consecutive patients with heartburn and/or regurgitation and a recent endoscopic assessment were enrolled. All patients underwent HRM to assess the EGJ and 10 single water swallows to evaluate the esophageal peristalsis and EGJ function. The tracings were analyzed and each EGJ was classified based on the Chicago Classification (CC) 3.0. EGJ Type I was further divided into Type IA, a complete overlap of LES and CD, and Type IB, a minimal separation, with LES located from the upper border of CD (in correspondence of pressure inversion point, 0.0 cm) to 1 cm above. The patients then underwent impedance-pH testing off-therapy. We measured the esophageal acid exposure time (AET), number of total impedance-detected reflux episodes and symptom association analysis using symptom association probability (SAP + if ≥95%) and symptom index (SI+ if ≥50%).
**Results:** We enrolled 168 [75M/93F; mean age 47 (18–81)] consecutive patients and identified 101 (60.1%) patients with Type I EGJ, 37 (22%) with Type II EGJ and 30 (17.9%) with Type III EGJ. Patients with Type III EGJ had an higher median number of reflux episodes, a greater mean AET and had more frequently a positive symptoms association compared to patients with Type II and Type I EGJ (Table 1). Overall, Type I subjects showed a positive MII-pH in 45.5% of cases, with the lowest value of number of reflux episodes, AET and positive symptom association. Using the sub-classification, we identified 54 (53.6%) Type IA and 47 (46.5%) Type IB subjects. Type IB had a higher number of reflux episodes (42 vs. 28, $p < 0.03$), a greater mean AET (4.7 vs. 2.9, $p < 0.05$) and a greater positive symptom association (54% vs. 26%, $p < 0.02$) compared to Type IA. Type IB morphology had a more frequent probability to show a positive MII-pH than Type IA (70.2% vs. 30%, $p < 0.001$).
**Conclusion:** With increasing separation between the LES and the CD patients had a gradually and significantly increase of reflux episodes and esophageal acid exposure. The sub-classification of EGJ Type I can be useful to better estimate an abnormal impedance-pH testing in GERD patients and it supports the role of the intra-abdominal LES segment in preventing reflux.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1545 EXTENDED BRAVO STUDIES (>48 HRS) OFFER AN ADDITIONAL DIAGNOSTIC YIELD OF GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD) IN PATIENTS WITH NORMAL MULTICHANNEL INTRALUMINAL IMPEDANCE-PH (MII-PH) STUDIES


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**Introduction:** MII-pH catheter studies measure both acid and non-acid reflux and are considered by some to be the gold standard in the diagnosis of GORD. Wireless pH capsule (Bravo) may increase the diagnostic yield of standard 24 hr catheter-based studies with prolonged monitoring by overcoming the limitation of day-to-day reflux variability and patients are able to perform activities of daily living without the discomfort of the nasal catheter.
**Aims & Methods:** This study aims to assess the additional diagnostic yield of extended Bravo recordings (up to 96 hours) in patients with negative 24 hr MII-pH results. A total of 44 patients with typical GORD symptoms but negative 24 hr MII-pH studies off proton pump inhibitor(PPI) were referred for Bravo capsule studies. Bravo studies were performed off PPI over an extended period beyond 48 hrs (up to 96 hrs). Bravo cases positive for AET were analysed using the Bravo 'Worst Day Analysis' (WDA) and 'Average Day Analysis' (ADA). Reference values for MII-pH and Bravo equivalent were adopted from internationally established studies (Table 1). Subgroup analyses were subsequently made on cohorts whose MII-pH showed normal AET with (A) normal number of total reflux events (TRE), (B) normal number of non-acid reflux (NAR) events and (C) increased number of NAR events. Subgroups (B) and (C) have normal number of acid reflux events. Statistical analysis was performed using SPSS V20.
Results:
Our study group (male = 14, female = 30) with a mean age of 48 years, successfully completed Bravo studies up to 96 hours in 77.3% and beyond 48 hours in 97.7%. Using the WDA and ADA respectively, Bravo (AET cut-off > 4.2%) captured an additional 59.1% and 43.2% of patients with increased AET ($p < 0.001$) in cases with normal AET on MII-pH. In MII-pH subgroups (A), (B) and (C), Bravo WDA was able to reveal an additional positive AET of 61.8%($p < 0.001$), 60.9%($p < 0.001$) and 50.0%($p = 0.016$) respectively compared to MII-pH while Bravo ADA showed a similar albeit smaller additional yield of 44.1% ($p < 0.001$), 43.5% ($p < 0.002$) and 35.7% (not significant). Results were similar using other internationally published Bravo AET limits of > 4.4% and > 5.3% (Table1). Inclusion of symptom reflux association in Bravo cases with increased AET also showed additional diagnostic yield over MII-pH ranging from 42.9–47.7% ($p \leq 0.031$) across all subgroups.
**Conclusion:** Extended Bravo studies managed to procure a diagnosis of GORD in more than half of cases with an initial normal MII-pH but persistent symptoms. Half of the patients with increased NAR events on MII-pH also showed positive acid reflux on prolonged testing using Bravo. This additional yield has the potential to alter diagnosis from functional heartburn/hypersensitive esophagus to GORD in difficult cases and affect management by intensifying acid suppression therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Table 1:** Increased Bravo Acid Exposure Time (AET) in normal MII-pH studies

| 24 hr MII-pH** | Bravo[1] (WDA) (% Increased AET) | Bravo[2] (WDA) (% Increased AET) | Bravo[3] (WDA) (% Increased AET) |
|---|---|---|---|
| Normal AET (n = 44) | 54.5% | 59.1% | 59.1% |
| Normal AET & normal TRE (n = 34) | 58.8% | 61.8% | 61.8% |
| Normal AET & normal NAR (n = 23) | 56.5% | 60.9% | 60.9% |
| Normal AET & Increased NAR (n = 14) | 50.0% | 50.0% | 50.0% |

N.S. = not significant; NAR = Non-acid Reflux; WDA = worst day analysis

**Cut-off values based on Shay et al. Am J Gastroenterol 2004; 99:1037

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## P1546 PROLONGED MEASUREMENTS IMPROVE THE ASSESSMENT OF GASTRO-ESOPHAGEAL JUNCTION BARRIER FUNCTION BY HIGH-RESOLUTION MANOMETRY IN GASTRO-ESOPHAGEAL REFLUX DISEASE

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**Introduction:** Aetiology of gastro-esophageal reflux disease (GERD) is multifactorial, but incompetence of the esophagogastric junction (EGJ) appears to be of crucial importance. Established manometric metrics for assessment of EGJ contractility and barrier function are sub-optimal, potentially because they are based on a very brief (up to 30 s), not necessarily representative section of the manometric investigation.

**Aims & Methods:** This prospective, case-control study aimed to test the performance of a novel, high-resolution manometry (HRM) parameter reflecting EGJ function over a prolonged period of time in the assessment of patients with suspected GERD.Patients with reflux symptoms and healthy controls (HC) underwent HRM with ten water swallows and 24-hour pH ± impedance measurements. EGJ morphology [1], lower esophageal sphincter pressure integral (LES-PI) [2], EGJ-contractile integral (EGJ-CI) [3] were compared with total-EGJ-CI, a novel parameter summarizing EGJ contractility during the entire HRM protocol (~ 5 min). Interaction with peristaltic function assessed by distal contractile integral (DCI) was evaluated. Esophageal acid exposure ≥ 4.2%/24 h (A-Reflux-pos) or ≥ 73 reflux episodes in 24 h (V-Reflux-pos) were considered pathological.

**Results:** 65 HC and 452 patients completed HRM, 380 (84%) patients underwent ambulatory reflux-monitoring. LES-PI, EGJ-CI and total-EGJ-CI correlated with EGJ-morphology subtypes and mean DCI (all $P < .00001$). Only total-EGJ-CI was consistently lower in A-Reflux-pos and V-Reflux-pos subjects compared with HC and patients without GERD. Total-EGJ-CI was also the single best parameter for prediction of pathological reflux (optimal cut-off 47 mmHg*cm, AUC 0.746, $P < .0001$). This cut-off value, approximately 1 SD below the mean normal value, showed modest sensitivity 54% and PPV 46%, but good specificity 85% and NPV 89% for GERD diagnosis.

**Table 1:** HRM-Parameters in HC and subgroups of patients

| | HC (n = 64) | A-reflux-neg (n = 116) | A-reflux-pos (n = 122) | V-reflux-neg (n = 114) | V-reflux-pos (n = 28) |
|---|---|---|---|---|---|
| **LES-PI mmHg*cm*s** | 105 [31–185] | 87 [27–245] | 62*° [7–157] | 140 [59–273] | 72° [15–175] |
| **EGJ-CI mmHg*cm** | 63 [48–86] | 61 [35–86] | 49** [25–71] | 69 [47–87] | 46*°° [31–65] |
| **total-EGJ-CI mmH*cm** | 63 [51–78] | 62 [42–85] | 46**°° [24–68] | 68 [56–85] | 47**°° [38–64] |

Data are given as median [IQR], p-values are corrected for multiple comparisons. *$p < 0.05$ vs HC, **$p < 0.01$ vs HC, ° $p < 0.05$ vs reflux-negative, °° $p < 0.01$ vs. reflux-negative

**Conclusion:** Total-EGJ-CI, a new metric that summarizes EGJ contractility over time, allows an improved assessment of EGJ-barrier function. Pathological reflux is unlikely if this metric is within the upper two-thirds of the normal range. These findings underline the crucial importance of EGJ contractility for barrier function and reflux protection.

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J. Keller: JK: - funds for research from Given Imaging / Medtronic - honoraria for presentations and / or reimbursement for attending symposia and / or is a member of advisory boards for Given Imaging / Medtronic and Standard Instruments
All other authors have declared no conflicts of interest.

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## P1547 THE DIAGNOSTIC VALUE OF 24-HOUR AMBULATORY INTRAESOPHAGEAL PH-IMPEDANCE IN PATIENTS WITH LARYNGOPHARYNGEAL REFLUX SYMPTOMS COMPARED TO THOSE WITH TYPICAL SYMPTOMS

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**Introduction:** The diagnosis of laryngopharyngeal reflux (LPR) is currently based on a combination of the patient history with laryngoscopic or ambulatory pH and intraluminal impedance (MII-pH); however, none of these findings alone is specific for the diagnosis of LPR. We aimed to compare the baseline characteristics and esophageal baseline impedance (BI) values between patients with and without LPR symptoms.

**Aims & Methods:** We retrospectively analyzed data from the patients with LPR as study group and nonerosive reflux disease (NERD) patients without LPR as controls. All patients who performed esophagogastro-duodenoscopy, esophageal manometry and MII-pH were accepted for the analysis. Patients with a history of endoscopically documented hiatal hernia (> 2 cm), erosive esophagitis, Barrett esophagus, history of manometrically documented esophageal motility disorders, other ENT pathologies were excluded from analysis. All MII-pH parameters and BI were analyzed from six levels (3,5,7,9,15 and 17 cm above LES). We accepted proximal BI as the mean of 15 (Z2) and 17 (Z1) cm above Lower esophageal sphincter (LES) and distal BI as the mean of 3 (Z6) and 5 (Z5) cm above LES. Additionally, to determine the exposure levels of different esophageal segments, we analyzed the ratio of BI measurements between the proximal and distal segments of esophagus as the proximal to distal ratio. In addition to MII-pH parameters, we compared the proximal BI, distal BI and Proximal to distal ratio values between patients with LPR and patients without LPR.

**Results:** 123 patients with LPR and 49 NERD patients (controls) were included in this study. All MII-pH findings were not different between groups (Table 1). However, BI analysis showed that patients with LPR symptoms had significantly lower proximal BI values ($1997 \pm 51$vs $2245 \pm 109$, $p < 0.05$) and proximal-to-distal ratio ($1.28 \pm 0.05$ vs $1.53 \pm 0.09$, $p < 0.05$) than the control group (Table 1). But, distal BI was not different between groups.

**Table 1:** The multichannel intraluminal impedance and pH monitorization and Baseline impedance analysis of patients with and without LPR. The number of reflux episodes and amount of acid reflux were lower but not significant in patients with LPR symptoms. However, the proximal BI and Proximal to diatal ratio were significantly lower in patients with LPR (Data are expressed as Mean ± SEM, *$p < 0.05$,**$p < 0.01$. Proximal BI: Mean BI of 15 and 17 cm above LES; Distal BI: Mean BI of 3 and 5 cm of LES; Proximal to distal ratio: Proximal BI/Distal BI)

| | Patients with LPR Symptoms (n = 123) | Patients without LPR Symptoms (n = 49) |
|---|---|---|
| Acid Exposure time (%) | 6.8 ± 1.05 | 6.1 ± 0.81 |
| Total reflux Episodes (n) | 44.4 ± 2.4 | 52.0 ± 3.4 |
| Acid Reflux (n) | 28 ± 2 | 33.6 ± 2.6 |
| Weak/Non-acid reflux | 15.7 ± 1.3 | 18.6 ± 2.06 |
| Proximal Reflux rate (%) | 33.4 ± 1.8 | 33.8 ± 3.7 |
| Proximal BI (Mean Z1 + Z2) | 1997 ± 51* | 2245 ± 109 |
| Distal BI (Mean Z5 + Z6) | 1809 ± 64 | 1666 ± 111 |
| Proximal to distal ratio | 1.28 ± 0.05** | 1.53 ± 0.09 |

**Conclusion:** LPR represents one of the most difficult disorders on the GERD spectrum, both in terms of diagnosis and treatment. There are currently no established diagnostic criteria, and a strong need. We found that patients with pathologic LPR symptom scores have lower proximal BI levels and lower proximal-to-distal ratios, which may reflect the proximal mucosal noxious effect of the refluxate. These results may indicate that LPR symptoms may be due to chronic acid exposure in the proximal segments of esophagus, and the proximal-to-distal ratio may be used as a new metric for diagnosis. Prospective studies are needed to confirm or refute this metric.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1548 SHOULD MEALS BE BLOCKED DURING AMBULATORY PH MONITORING?


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**Introduction:** The pH sensor cannot differentiate retrograde from anterograde bolus movement. Physiologists often block meals in pH studies to reduce the artefact of acid-containing food/fluids; however there is no clear evidence with regards to the appropriateness of this practice. The aim of this study was to compare results of ambulatory pH monitoring without and with meals blocked in patients being investigated for reflux symptoms.
**Aims & Methods:** Standard pH parameters were compared without and with meals blocked in consecutive patients presenting to University College London Hospital Oesophageal Unit, a tertiary referral centre. T-test was used for quantitative and chi square for qualitative variables. Results are presented as mean-standard deviation(SD)
**Results:** pH studies for 99 patients with reflux-like symptoms were collected prospectively over 3 months. Under 17 hour recordings ($n=2$) or studies ON acid-reducing therapy ($n=6$) were excluded. Mean age of the 91 remaining patients (M31:F60) was $50\pm15$ years. Time spent without and with meals blocked was $1388\pm100$ and $1243\pm114$ minutes respectively ($p<0.001$); $145\pm111$ min difference. There was no difference in the quantitative or qualitative Total reflux (% time pH < 4; TR), Upright reflux (UR) or Supine Reflux (SR) when analysed without and with meals excluded.(Table) At individual level, meal exclusion changed TR/UR/SR to become negative in 4 and positive in 2 patients; average 5% (range 2.5–23 min) of the mealtime was taken up swallowing acid-containing products. Food diary occasionally provided guidance, although quality of self-reports was widely variable.

| | Meal Included | Meal Excluded | p | # positive (meal included) | # positive (meal excluded) | p |
|---|---|---|---|---|---|---|
| Total Reflux | 5.95 (7.05)% | 6.09 (7.73)% | 0.461 | 42 | 41 | 1.000 |
| Upright Reflux | 6.00 (6.28)% | 6.38 (6.87)% | 0.382 | 33 | 32 | 1.000 |
| Supine Reflux | 5.91 (11.58)% | 5.85 (11.61)% | 0.486 | 44 | 43 | 1.000 |

There was no difference in qualitative ($p=0.538$) or quantitative ($p=0.338$) Symptom Index (SI) when meals were not blocked (12 positive; mean $16.9\pm22.6\%$) compared to when meals were blcked (16 positive; mean $18.4\pm25.4\%$). Also there was no difference in any pH parameters between the two groups with all simptoms pooled, or with typical (heartburn, regurgitation, chest pain; $n=59$) and atypical symptoms (laryngopharyngeal reflux, cough, belch, dysphagia; $n=33$) analysed separately ($p=$ NS for all). Furthermore there was no difference in any pH parameter when results were analysed with ($n=43$) or without ($n=48$) a hiatus hernia ($p=$ NS for all).
**Conclusion:** In 93% of patients, routine blocking of meals had no impact on the final report. In a small minority, the artefact of swallowing acidic products as well as shortening of the 24 hour study to exclude meals (average ≥2 hours) can also change results from positive to negative and vice versa.
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All other authors have declared no conflicts of interest.

## P1549 HOX GENE EXPRESSION IN BARRETT'S ESOPHAGUS RESEMBLES THAT OF THE COLON, CAN BE MODULATED BY ACID AND BILE EXPOSURE, AND INDUCES BARRETT'S SPECIFIC GENE PRODUCTS


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**Introduction:** Barrett's Esophagus (BE) is a metaplastic and precancerous condition. It is induced by bile and acid reflux and defined by the presence of intestinal-type tissue in the esophagus. The morphology of this tissue resembles a posterior phenotype, as observed in the colon. Identifying the cause of this positional misspecification can lead to a better understanding of BE pathophysiology. HOX genes encode master regulators of anterior to posterior specification in organogenesis and tissue homeostasis. The 3' to 5' sequence of HOX genes corresponds to the sequence in which they act along the anterior to posterior axes of the body. This property is termed collinearity and links clustering to function. Acquired deregulation of HOX genes during adulthood is linked to carcinogenesis. However, HOX collinearity has not been thoroughly investigated in the human gut, nor in BE.
**Aims & Methods:** The aim of this study was to characterize HOX expression along the gut and in BE in order to compare expression patterns. Furthermore, potential causes and consequences of HOX gene aberrations were investigated. Expression of 39 HOX genes was determined by RT-qPCR in tissues taken from 9 locations along the gut of 3 control patients, in squamous and BE tissues of 13 BE patients, and in esophageal adenocarcinoma (EAC) biopsies of 9 patients. Expression of 11 HOXA cluster genes were determined in columnar lined esophagus without intestinal metaplasia, and in intestinal metaplasia of the stomach. Squamous esophageal cell lines HET-1 A and EPC2-hTERT were exposed to acid and bile to simulate gastro esophageal reflux disease (GERD). HOXA13 RNA-ISH was performed and HOXA13 was transduced and overexpressed in EPC2-hTERT.
**Results:** HOX cluster gene expression differed significantly along the gut. In general, HOX gene expression was highest in the colon with exception of the HOXC cluster expression. HOXA cluster gene expression was the highest compared to other clusters. The most posterior highly expressed HOX cluster members in the esophagus of the control patients were A7, B7, C8, and D8 and in the rectum A13, B13, C10, and D13. BE tissue was characterized by upregulation of HOXA10, 11, and 13, B3, 6, 7, 8, 9, and 13, and C6, 9, 10, and 11. Downregulated in BE were HOXA1, 4, and 7. For clusters A and B, the HOX pattern observed in BE was similar to that seen in colon epithelium. The HOXA cluster genes, determined in columnar lined esophagus without intestinal metaplasia, i.e. without goblet cells, showed similar aberrations to those found in BE with goblet cells. In fact, aberrant expression of HOXA cluster genes could be detected in the squamous epithelium taken 5 cm above the z-line of BE patients, when compared with control patients. Furthermore, the aberrant HOX gene expression pattern found in BE, remains present in its sequela EAC. Intestinal metaplasia of the stomach has a similar HOX gene expression when compared to intestinal metaplasia of the esophagus. HOXA and B cluster expression patterns adhere to the collinear property and have similar expression patterns in BE when compared to the colon. Therefore, the posterior members of these clusters could well be responsible for the posterior morphology observed in BE. HOXA13, highly overexpressed in BE and intestinal metaplasia of the stomach, was chosen for further studies. HOXA13 mRNA was visualized in the epithelial cells of BE tissue, its sequela EAC, and intestinal metaplasia of the stomach. Exposure of two esophageal cell lines to acid and bile led to up regulation of HOXA13. Furthermore, induced overexpression of HOXA13 in turn upregulated expression of KRT7 and COX2, both involved in BE.
**Conclusion:** HOX gene collinearity is present along the adult human gut. HOX gene rearrangements are found in BE and intestinal metaplasia of the stomach, both resulting in a similar colon like HOX expression pattern. Aberrant HOX expression occurs early in the pathogenesis of BE and remains present in its sequela EAC. Acid and bile exposure leads to upregulation of the posterior HOXA13 in an in vitro GERD model. Furthermore, HOXA13 overexpression induces BE specific gene products.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1550 EPITHELIUM TYPE AND DISTANCE FROM THE LOWER OESOPHAGEAL SPHINCTER SHOW INFLUENCE ON MUCOSAL BASELINE IMPEDANCE IN BARRETT'S OESOPHAGUS

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**Introduction:** Low distal mucosal baseline impedance (BI) can be considered a proxy of damaged mucosal integrity [1] and has been associated with acid hypersensitivity [1,2]. Furthermore, BI is known to be low in Barrett's oesophagus [3]. However, the influence of epithelium type and distance from the lower oesophageal sphincter (LOS) on mucosal BI are less well studied.
**Aims & Methods:** We aimed to characterize distal mucosal BI in Barrett's oesophagus in relation to epithelium type (columnar vs. squamous) and distance from the LOS. Twenty-six patients with Barrett's oesophagus (mean age: $64.2 \pm 7.3$ years) were compared with 12 healthy controls (mean age: $54.9 \pm 10.7$ years). Barrett segment length was measured endoscopically. A pH-impedance probe with six impedance channels and one pH channel was placed in the oesophagus. After adjustment to the probe, mucosal BI 17, 15, 9, 7, 5, and 3 cm above the LOS was measured for five minutes. This measurement was followed by a standard ambulatory pH measurement 5 cm above the LOS. Based on endoscopy findings, BI data for squamous and columnar epithelium in patients were analysed separately, while data from channels overlapping both types of epithelium were excluded.
**Results:** Patients had a mean Barrett segment length of $5.3 \pm 4.2$ cm circular and $6.6 \pm 4.0$ cm maximal. At 5 cm above the LOS, BI in squamous epithelium was 33% lower in patients with Barrett's oesophagus ($n = 7$) than in controls ($P = 0.001$). Comparing epithelium types in patients, BI was 80% higher in patients having squamous ($n = 7$) compared with those having columnar epithelium ($n = 15$) at 5 cm above the LOS ($P < 0.001$). In patients, BI overall decreased linearly with shorter distance from the LOS ($P < 0.001$). This was also true in separate squamous ($P < 0.001$) or columnar epithelium in patients ($P < 0.001$), but not in controls ($P = 0.6$). In patients, BI decreased linearly with increasing maximal Barrett segment length ($P < 0.001$), which was also true in separate columnar epithelium ($P = 0.003$). This correlation was not present in separate squamous epithelium in patients ($P = 0.6$). Ambulatory acid exposure was greater in patients than in controls ($P = 0.04$). Overall, mucosal BI decreased with greater acid exposure ($P = 0.009$).
**Conclusion:** Distal squamous mucosal BI in patients with Barrett's oesophagus was lower compared with columnar mucosa in patients and compared with healthy controls. Furthermore, BI generally decreased with shorter distance from the LOS and with greater acid exposure. Thus, we suggest that greater distal oesophageal acid exposure in Barrett's oesophagus impairs mucosal integrity as measured by a lower BI. This mucosal damage may partly explain the acid hypersensitivity reported in patients with Barrett's oesophagus [2].
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1552 IMMUNOHISTOCHEMICAL BIOMARKERS FOR RISK STRATIFICATION OF NEOPLASTIC PROGRESSION IN BARRETT ESOPHAGUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Introduction:** Barrett's esophagus (BE) is the precursor lesion of esophageal adenocarcinoma (EAC). None of the current clinical or endoscopic criteria are able to accurately predict which patients will progress from BE to EAC. Immunohistochemical (IHC) biomarkers can be applied to intact histological morphology, and are relatively easy applicable in daily practice.
**Aims & Methods:** This study aimed to provide a systematic review and meta-analyses of all published studies on IHC biomarkers as predictors of neoplastic progression in BE. Thereto, MEDLINE, EMBASE, Web of Science, CENTRAL, Pubmed publisher, and Google scholar were searched. All studies on IHC biomarkers in BE progression were included. Two authors independently extracted data. An inverse variance random-effect model was used. Meta-analyses were performed for biomarkers studied more than once. Pooled estimates of effect were calculated and results investigated for statistical heterogeneity by the I-squared test ($I^2$). If enough studies were present, sensitivity analyses and sub-analyses were performed. The sub-analyses were performed to investigate whether IHC biomarkers had a predictive value independent of the presence of LGD.
**Results:** IHC biomarkers studied more than once were p53, Cyclin A, Cyclin D, and aspergillus oryzae lectin (AOL). The IHC biomarker investigated most frequently was p53, it was included in 12 studies, which contained 2023 patients, of which 372 cases. In the meta-analyses aberrant p53 IHC staining was significantly associated with the risk of neoplastic progression in BE patients with an OR of 4.15 (95% CI 1.96 to 8.81). A sub-analysis stratifying for the presence or absence of LGD showed that aberrant p53 IHC staining was associated with neoplastic progression with an OR of 4.13 (95% CI 2.36 to 7.21). This association was confirmed for both non-dysplastic BE, and BE with low grade dysplasia individually. Of the other IHC biomarkers Cyclin A (OR 1.54, 95% CI 0.62 to 3.79), Cyclin D (OR 1.87, 95% CI 0.17 to 20.63), and AOL, only AOL appeared to be able to predict neoplastic progression in BE patients with an OR of 3.04 (95% CI 2.05 to 4.49).

Overview of meta-analyses performed

| Analysis | Studies | Cases | Controls | OR | 95% CI | $I^2$ |
|---|---|---|---|---|---|---|
| p53 (main) | 12 | 372 | 1651 | 6.67 | 3.64–12.22 | 55% |
| p53 (excluded small studies) | 6 | 323 | 1287 | 4.40 | 2.30–8.40 | 63% |
| p53 (also excluded unadjusted ORs) | 5 | 289 | 1124 | 4.15 | 1.96–8.81 | 68% |
| p53 (also excluded abstracts) | 4 | 149 | 985 | 5.23 | 2.09–13.03 | 64% |
| p53 (only ORs stratified for histology) | 7 | 316 | 1221 | 4.13 | 2.36–7.21 | 41% |
| p53 (only non-dysplastic BE) | 2 | 61 | 659 | 6.12 | 2.99–12.52 | 0% |
| p53 (only BE with LGD) | 4 | 37 | 145 | 8.64 | 3.62–20.62 | 0% |
| Cyclin A | 3 | 235 | 415 | 1.54 | 0.62–3.79 | 71% |
| Cyclin D | 2 | 46 | 212 | 1.87 | 0.17–20.63 | 87% |
| AOL | 2 | 204 | 369 | 3.04 | 1.74–4.49 | 0% |

**Conclusion:** In conclusion, p53 is the most studied IHC biomarker for neoplastic progression in patients with BE. Aberrant p53 IHC is significantly associated with an increased risk of neoplastic progression in BE patients, which appears to be independent of dysplasia grade.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Abstract No: P1553**

| | LogRank p-value |
|---|---|
| Female (19/158) | 0.561 |
| Age at least 58 years (n = 122/159)<br>Age at least 65 years (n = 78/159)<br>Age at least 73 years (n = 41/159) | 0.172 0.914 0.610 |
| prior EMR (n = 90/159) | 0.196 |
| High grade dysplasia or adca (n = 136/155)<br>Adenocarcinoma (n = 58/155) | 0.391 0.469 |
| Prague C score at least 1 (n = 95/159)<br>Prague C score at least 2 (n = 79/159<br>Prague C score at least 4 (n = 46/159) | 0.674 0.409 0.729 |
| Prague M score at least 2 (n = 137/159)<br>Prague M score at least 5 (n = 80/159)<br>Prague M score at least 6 (n = 51/159) | 0.546 0.473 0.508 |
| Distance diagraphm Z line at least 1 cm (n = 131/159)<br>Distance diagraphm Z line at least 2 cm (n = 111/159)<br>Distance diagraphm Z line at least 4 cm (n = 44/159) | 0.481 0.353 0.999 |
| At least one RFA session (n = 97/159) At least two RFA sessions (n = 39/159) | 0.919 0.566 |

## P1553 RADIOFREQUENCY ABLATION IN BARRETT'S ESOPHAGUS: ARE THERE ANY FACTORS PREDICTING LONG TERM REMISSION OF INTESTINAL METAPLASIA?

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**Introduction:** Radiofrequency ablation (RFA), combined with endoscopic mucosal resection (EMR) of visible lesions, can be used as a primary treatment for low-grade dysplasia (LGD), high-grade dysplasia (HGD) and early adenocarcinoma (EAC) in Barrett's esophagus (BE). Success rates for long-term complete remission of intestinal metaplasia (CR-IM) outside clinical trials have been reported to be 62%.

**Aims & Methods:** In this study we wanted to assess possible risk factors for recurrence of IM after CR-IM is achieved. Between February 2008 and August 2015, data from 7 centers performing RFA were prospectively collected in the Belgian RFA registry. CR-IM was defined as biopsy-proven absence of intestinal metaplasia (IM) and dysplasia with endoscopic remission of BE. Follow-up (FU) was calculated from the time CR-IM was achieved. A univariate analysis was performed to assess and detect possible risk factors for recurrent disease in patients with a minimum of 6 months FU. We assessed demographic, disease related and procedure related factors.

**Results:** 279 patients (mean age 65; 84.5% men) were included in the Belgian RFA registry. 60% received EMR prior to RFA. 44 patients were still under treatment at the time of analysis, 18 discontinued treatment and treatment failed in 23 patients. CR-IM was achieved in 194 patients (ITT: 82.5%, PP: 89.4%). 185 entered FU (median FU time: 735 days). Recurrent disease with biopsy proven intestinal metaplasia under the neo Z-line occurred in 63 patients (mean time to recurrence 445 days + /- 362) and there was sustained remission in 122 patients (ITT: 63%, PP: 66%). Histology of recurrence was IM (38), HGD/adenocarcinoma (17), LGD (7) and unknown (1). 158 patients (mean age 65, 88% men) with a FU of more than six months, were included in the univariate analysis to assess possible risk factors for recurrent disease. No significant association was found between recurrence of disease and sex, age, prior EMR, worst histology before treatment, length of the BE (Prague classification), size of hiatal hernia and number of RFA sessions (see table). As a result, no multivariate analysis could be performed.

**Conclusion:** In this analysis of the multicenter Belgian RFA registry we found sustained CR-IM rate of 66%. We could not identify patient, disease or procedure related risk factors to predict an increased risk for recurrence. Therefore surveillance endoscopy after treatment and ablation of dysplastic Barrett's remains necessary.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1554 DURABILITY OF RADIOFREQUENCY ABLATION IN BARRETT'S OESOPHAGUS WITH DYSPLASIA: A SEVEN-YEAR AUSTRALIAN EXPERIENCE

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**Introduction:** Radiofrequency ablation can eradicate dysplasia and intestinal mataplasia in patients with dysplastic Barrett's Oesophagus.

**Aims & Methods:** This prospective cohort study aims at assessing the long-term eradication of dysplasia and intestinal metaplasia, and durability of neosquamous epithelium in patients with dysplastic Barrett's Oesophagus treated with radiofrequency ablation (RFA) in a metropolitan tertiary referral centre. All patients with dysplastic Barrett's Oesophagus treated with RFA from November 2008 to February 2016 were identified. Patients were followed up for a mean time of 3.3 years. Follow up of eradication of dysplasia and intestinal metaplasia was measured from the first RFA treatment session. Durability of neosquamous epithelium was measured from the first documentation of dysplasia or intestinal metaplasia eradication.

**Results:** RFA treatment was used in 153 patients with dysplastic Barrett's Oesophagus. Of these patients, 134 (88%) were male with a mean age of 72. At the time of referral, 19 (12%) patients had early cancer (EC), 73 (48%) patients had high grade dysplasia (HGD) and 61 (40%) patients had low grade dysplasia (LGD). One hundred and twelve (73%) patients also underwent endoscopic mucosal resection (EMR). After 1 year, 102 of 116 (88%) patients had complete eradication of all dysplasia (CE-D) and 68 of 116 (59%) had complete eradication of intestinal metaplasia (CE-IM). After 2 years, 71 of 79 (90%) patients had CE-D and 56 of 79 (71%) patients had CE-IM. After 3 years, there was CE-D in 43 of 45 (96%) patients and CE-IM in 35 of 46 (76%) patients. By 4 years, 26 of 26 (100%) patients had CE-D and 20 of 26 (77%) patients had CE-IM. After 5 years, 17 of 17 (100%) had CE-D and 15 of 17 (83%) had CE-IM. Kaplan Meier analysis showed that at 3 years, dysplasia remained eradicated in 88% of patients while intestinal metaplasia remained eradicated in 67% of patients. At 5 years, dysplasia remained eradicated in 84% of patients and intestinal metaplasia remained eradicated in 56% of patients. There were 15 patients with relapse of dysplasia; 8 (53%) patients had recurrence of LGD, 6 (40%) patients with HGD and 1 (7%) patient had recurrence of EC. Thirteen of these 15 (87%) patients had subsequent CE-D with ongoing RFA and EMR. There were no deaths related to relapse of disease. Of the 33 patients with relapse of intestinal metaplasia, 13 (39%) also had recurrence of visible Barrett's on gastroscopy. Twenty-one (68%) patients had subsequent CE-IM with further RFA therapy.

**Conclusion:** Majority of patients with dysplastic Barrett's Oesophagus treated with RFA therapy remain in remission. However, there is still a significant rate of recurrence of dysplasia and intestinal metaplasia. This indicates that long term surveillance of patients with dysplastic Barrett's Oesophagus is mandatory.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1555 MULTIFOCAL NITROUS OXIDE CRYOBALLOON ABLATION WITH OR WITHOUT ENDOSCOPIC MUCOSAL RESECTION (EMR) FOR TREATMENT OF NEOPLASTIC BARRETT'S ESOPHAGUS: PRELIMINARY RESULTS OF A PROSPECTIVE CLINICAL TRIAL IN TREATMENT-NAÏVE AND PREVIOUSLY ABLATED PATIENTS

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**Introduction:** Radiofrequency ablation (RFA) is highly effective for treatment of BE. However, post-ablation pain, strictures, and bleeding can develop. Endoscopic cryotherapy (Cryo) can successfully eradicate neoplastic BE, including refractory disease, with low stricture rate and no bleeding. A new portable battery-powered system (cryoballoon focal ablation system (CbFAS)(1) with a small hand-held device converts liquid nitrous oxide to gas resulting in an ice patch of approximately 2 $cm^2$. The gas is contained within a low pressure compliant through-the-scope balloon making contact with the mucosa, obviating the need for intraluminal suction.

**Aims & Methods:** We aimed to determine the safety and efficacy of nitrous oxide Cryo using a CbFAS for eradication of neoplastic Barrett's esophagus. In a single center, prospective single-arm clinical trial, consecutive BE patients with confirmed neoplasia (LGD, HGD, and/or T1aECA) without prior therapy (''treatment-naïve'') or persistent/recurrent disease despite prior therapies (''previously ablated'') were treated with CbFAS at dose 10 seconds of ice per site. EMR was performed prior to Cryo for lesions. Ablations were delivered from distal to proximal, beginning at the gastric cardia/GE junction, to include all visible BE with WLE-HRE and NBI, followed by treatment of skip areas. Treatments were repeated every 10–12 weeks until eradication of intestinal metaplasia (IM). Patients were included if there was biopsy-proven BE > 1 cm (Prague M1 or greater), no limit on length. Maximum number of ablations for each treatment session was 24.

**Results:** 40 patients (15 with prior ablation) with low-grade dysplasia (LGD n = 13), high-grade dysplasia (HGD n = 24) or intramucosal cancer (n = 3) have had 83 treatments (Table 1). EMR rate was 35%. Median number of cryoablations was 9.8 per session (IQR 6–21). To date, all procedures were successfully completed (all targeted sites ablated) except for 3 with balloon migrations across strictures leading to incomplete ablation, subsequently successful. Mean ablation and procedure times were 18.3 (IQR 13–31) and 30.5 (24–44) minutes, respectively. 24 enrolled patients were evaluable with at least 1 negative set of biopsies from the GEJ to prior Z line level. The remaining 16 patients have completed treatment and are awaiting follow-up biopsy procedures. Median number of ablation procedures was 2 (IQR 1–3, maximum 4). Short-term complete response for all dysplasia (CRD) to date is 10/11(90%) of treatment-naïve and 13/13(100%) previously ablated patients. To date, combined with EMR for nodular BE, overall CR-D and CR-IM rates are 23/24(96%) and 23/24(96%), respectively, with no difference by BE length or history of prior ablation. There were 2 minor balloon tears and 1 upper GI bleeding due to ulcers in a patient taking aspirin. Post-ablation pain requiring narcotics was reported in 10/40 (25%), majority post-procedure while in PACU, only 2 (5%) requiring narcotic after day 1. Immediate post-ablation pain score (Likert scale 1–10) was 1.9 (IQR 0–2.5) but decreased 0 by 24 hours (IQR 0–2). 4 patients developed mild dysphagia (1 resolved, 2 inflammatory stenoses dilated at next scheduled follow-up procedure). The one treatment failure was a patient with extensive multifocal nodular intramucosal cancer and HGD in a treatment-naive BE Prague C9M9 who had multiple EMR (total 50% circumferential) and developed high-grade stricture requiring 2 interval dilations and rescue APC. The patient opted to have surgery, results pending. No patient has had a persistent symptomatic stricture, including 10 with a pre-existing post EMR/RFA stricture. No buried BE has been detected.

**Conclusion:** Multifocal nitrous oxide cryoballoon ablation is a promising, safe, and potentially effective endoscopic treatment for primary or rescue therapy of BE-associated neoplasia. Device improvements are ongoing and larger multicenter comparative clinical trials are planned to assess long-term safety and efficacy.

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All other authors have declared no conflicts of interest.

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## P1556 THE CASE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION IN BARRETT'S CANCER: OUTCOMES FROM A 100 PATIENT SERIES

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**Introduction:** Endoscopic resection (ER) followed by radiofrequency ablation is advocated as the treatment of choice for management of early Barrett's neoplasia. Endoscopic submucosal dissection (ESD) is an emerging technique for resection of early Barrett's cancers that enables removal of the cancer en bloc and can lead to lower recurrence rates. However, it may be associated with a higher risk of complications including bleeding, perforation and stricture formation.

**Aims & Methods:** The aim of this study was to report safety and efficacy outcomes from a series of 100 patients undergoing ESD for suspected Barrett's cancer. This was a prospective analysis of outcome and follow up data collected from the Barrett's endoscopic resection database in our tertiary centre between 2008–2016. Patients underwent ablation of the residual Barrett's oesophagus only once clear of neoplasia on biopsy after at least 2 follow ups (6–12 months post resection).

**Results:** 100 ESD resections for suspected Barrett's cancers were performed in this time period by a single expert endoscopist (PB). The mean age of this cohort was 72 years with a mean Barrett's circumference (C) of 4 cm and length (M) of 6 cm. The mean length of follow up was 1.7 years. 74% of the lesions were classified as Paris IIA and Is lesions. The mean circumferential extent of resection involved 1/3 of the circumference with an average procedure time of 81 minutes. 67% of the patients in this series had intramucosal cancer and 16% had submucosal cancer on final histology. 11% had high-grade dysplasia and 6% had low-grade dysplasia. The endoscopic prediction of cancer was accurate in 83% of cases.

Outcomes of ESD for Suspected Barrett's Cancer

| | En bloc resection rate | R0 resection for cancer* | Complication rate** | Recurrence of cancer/HGD on endoscopic follow up | Cure rate of neoplasia after further ER |
|---|---|---|---|---|---|
| Number of patients(%) | 91/100 (91%) | 63/83 (75.9%) | 3/100 (3%) | 15/85 (17.6%) | 79/85 (92.9%) |

*R0 resection for cancer = clear of cancer at both horizontal and deep margins
**Complication rate: Bleeding (1%), Perforation (0%), Strictures (2%)

Means comparison testing demonstrated that the size of the lesion was a significant predictor of R1 resection (mean size in R0 group 30.4 mm versus R1 group 39.6 mm, p = 0.02). 85% of the patients were entered into endoscopic follow up and recurrence of cancer or high grade dysplasia was identified in 15 patients. 13/15 (86.7%) underwent further endoscopic resection and are now clear of cancer whilst 2 went on to have radiotherapy in view of poor fitness for surgery. Ultimately, an endoscopic cure was achieved in 79/85 (92.9%) of patients on the endoscopic follow up pathway even prior to being offered ablative therapy.

**Conclusion:** This is the largest reported series of ESD demonstrating its safety and efficacy as a resection technique for suspected Barrett's cancer. 85% of patients in this series successfully avoided more invasive surgery/oesophagectomy. The recurrence rate of Barrett's neoplasia is low following ESD and almost all recurrences were managed successfully with further endoscopic resection. ¾ of patients with Barrett's cancer achieved R0 resection. This was reflected in an even higher overall endoscopic cure rate which further strengthens the case for ESD in Barrett's cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1557 SAFETY OF RADIOFREQUENCY ABLATION FOLLOWING ENDOSCOPIC RESECTION IN BARRETT'S NEOPLASIA: DOES RESECTION METHOD MATTER?

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**Introduction:** The current standard of treating Barrett's neoplasia is resection of visible lesions followed by ablative therapy to the Barrett's segment. Endoscopic mucosal resection (EMR) is the conventional method of resection although there is growing evidence for the use of endoscopic submucosal dissection (ESD). Radiofrequency ablation (RFA) is a safe and effective ablation technique but carries a risk of complications including bleeding, stricture and perforation. ESD is associated with much deeper submucosal dissection then EMR, resulting in a deeper and thicker scar. This has been a cause for concern whilst performing RFA after ESD and experts have raised the possibility of higher stricture or perforation rates with RFA after ESD.

**Aims & Methods:** Aims: To compare the safety and efficacy of radiofrequency ablation following EMR and ESD and to ascertain if there are any significant differences. Methods: An electronic database (from 2007–2015) of all patients who had endoscopic resections (EMR or ESD) for Barrett's neoplasia followed by RFA was analysed. Data was collected on patient demographics, Barrett's length, lesion size, number of ablations required and follow up period. The

clearance of neoplasia (high grade dysplasia/intramucosal cancer) was also recorded (CE-N) along with procedural complications including bleeding, perforation and strictures.
**Results:** There were 30 patients in the EMR + RFA group (average age 73.1 years) compared to 19 in the ESD + RFA group (average age 74.6 years). Patients received circumferential ablation (HALO 360) or focal ablation (HALO 90/60/Ultra) depending on the extent of residual Barrett's oesophagus post endoscopic resection. Table 1 shows the outcome of RFA following EMR or ESD. ESD was started in our institution later than EMR and that is reflected in lower numbers and shorter follow up in the ESD cohort but it is otherwise a well matched population.

**Table 1:** Outcome of RFA following EMR vs ESD

| | EMR + RFA | ESD + RFA |
|---|---|---|
| Number of patients | 30 | 19 |
| Mean follow up (years) | 4.1 | 1.6 |
| Mean Barrett's length (cm) | 7.4 | 7.1 |
| Mean lesion size (mm) | 20.4 | 26.7 |
| Mean number of ablations | 1.9 | 1.7 |
| CE-Neoplasia | 93.3% | 94.7% |
| Bleeding (n, %) | 0 | 1 (5.3%) |
| Perforation (n, %) | 0 | 0 |
| Stricture (n, %) | 2 (6.7%) | 0 |

**Conclusion:** This is the first UK series reporting on the safety and efficacy of RFA after ESD. RFA following ESD or EMR is equally safe and effective and the endoscopic resection method is not a significant factor when planning ablation therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1558 WHAT IS THE CLINICAL IMPORTANCE OF AN INCIDENTAL IRREGULAR Z LINE? A LONG-TERM FOLLOW- UP STUDY

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**Introduction:** Barrett's esophagus (BE) is a well-known complication of gastro-esophageal reflux disease (GERD). In a previous study, we described a high prevalence of specialized intestinal metaplasia (SIM) in patients with an incidental irregular Z line. However, the clinical importance of SIM, and particularly, the development of BE or dysplasia during long-term follow-up in patients with an incidental irregular Z line is unclear.
**Aims & Methods:** We aimed to evaluate the long-term development of BE, dysplasia and esophageal adenocarcinoma in patients diagnosed with an irregular Z line, with or without SIM, on routine upper endoscopy. Methods: In our previously described cohort, 166 out of 2000 consecutive patients (8%) were diagnosed with an incidental irregular Z line. Of those with irregular Z line, 43% were identified with SIM. In this prospective, continuation study, electronic medical files of all patients who were previously diagnosed with an irregular Z line were re-assessed after a median follow-up of 68 months. Patients with an irregular Z line were divided into two groups: Patients with SIM (positive SIM group) and without SIM (negative SIM group). The prevalence of long-term development of BE, dysplasia and esophageal adenocarcinoma were compared between the groups.
**Results:** In the present study, at least one follow-up upper endoscopy was performed in 102 (61%) patients with an irregular Z line. Of those who were available for follow-up, 50 patients were identified with SIM during their first upper endoscopy (positive SIM group), and 52 patients did not have SIM during their first upper endoscopy (negative SIM group). Barrett's esophagus was evident in 16 positive SIM patients (16/50 [32%]) and in two negative SIM patients (2/52 [4%]), $p < 0.005$. Four (8%) positive SIM patients were found to have BE with low grade dysplasia (three with long segment ( > 3 cm) and one with short segment BE: Both negative SIM patients developed short segment BE without dysplasia ($p < 0.005$). None of the patients who were available for follow-up developed high grade dysplasia, or esophageal adenocarcinoma.

**Table 1:** Long-term follow-up endoscopic and pathologic findings of the available cohort (102 patients) with an incidental irregular Z line

| Number | Positive SIM Group 50 | Negative SIM Group 52 | p-value |
|---|---|---|---|
| Male gender N (%) | 39 (78) | 39 (75) | NS |
| Age (mean ± SD) | 64 ± 11 | 60 ± 15 | NS |
| Barrett's Esophagus (BE) N (%) | 16 (32) | 2 (4) | < 0.005 |
| Low grade dysplasia N (%) | 4 (8) | 0 | < 0.005 |

**Conclusion:** After a median 5 years follow-up, BE and low grade dysplasia were diagnosed more frequently in patients who had a prior irregular Z line with SIM, than in those without SIM.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1559 COST-EFFECTIVENESS OF ENDOSCOPIC TREATMENT WITH RADIOFREQUENCY ABLATION FOR PATIENTS WITH BARRETT'S ESOPHAGUS AND LOW GRADE DYSPLASIA IN SPAIN

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**Introduction:** While there is a strong agreement on how to treat patients diagnosed with Barrett's Oesophagus (BE) and High Grade Dysplasia (HGD) or Early Adenocarcinoma (EAC), the optimum treatment choice for patient diagnosed with Low Grade Dysplasia (LGD) is still widely discussed.
**Aims & Methods:** The objective of this study is to assess the cost-effectiveness of endoscopic treatment for LGD patients compared with standard of care in Spain. A 15-year horizon Markov model was developed to represent the evolution of the disease in 65-year-old patients diagnosed with BE and LGD in Spain. The therapeutic strategies compared were: immediate endoscopic treatment based on radiofrequency ablation (RFA) with endoscopic mucosal resection for visible, nodular areas followed by endoscopic surveillance vs. endoscopic surveillance alone. Patient treated with RFA eradicated dysplasia, both dysplasia and intestinal metaplasia (IM) or none according to recently published evidence by Phoa et al. (2014). The model considered six health states (1. Cured with antecedents – patients without dysplasia and IM or patients cured after surgical intervention; 2. BE without dysplasia – patients without dysplasia but with persistent IM; 3. LDG; 4. HGD; 5. EAC and 6. Death). Transition probabilities and utility values associated to each health state were obtained according to disease natural history from published literature and validated by three local clinical experts. Clinical management patterns and resource use were modelled according to the Spanish clinical practice and were obtained from clinical experts. Unit costs and pharmacologic costs were extracted from Spanish medical cost databases and expressed in euros of 2016. The National Health System perspective was considered, including the following costs: procedures and endoscopic surveillance cost, drug acquisition cost (ex-factory), surgical intervention, follow-up expenses and complications cost (perforation and stricture). An annual 3% discount rate was applied for costs and outcomes. One-way sensitivity analyses was performed to test the robustness of the model and uncertainty around base case parameters.
**Results:** Initiating treatment with RFA reduces the number of EAC progressions and avoids the need for oesophagostomy by 9%. Overall, for 65-year-old LGD patients, endoscopic treatment with RFA compared to endoscopic surveillance increases life expectancy by 0.08 life-years [0.54 Quality-Adjusted Life Years (QALY)] at an incremental cost of €9,346, that would mean an incremental cost-effectiveness ratio of €17,365 per QALY gained. Although cost-effectiveness of endoscopic treatment persisted in most of univariant scenarios, as expected, model outcomes resulted sensitive to the difference in inputs used to model the transition and quality of life of patients with LGD compared to patients with BE and no dysplasia or patients cured with antecedents.
**Conclusion:** The present evaluation indicates that endoscopic treatment with RFA is a cost-effective option compared to endoscopic surveillance only for the treatment of patients diagnosed with BE and LGD in Spain considering a willingness-to-pay threshold of €30,000 per QALY gained.
**Disclosure of Interest:** C. Collados: Medtronic Iberia SL employee
M. Álvarez Orozco: Medtronic Iberia SL employee
S. Şerip: Oblikue Consulting employee. Oblikue Consulting is an independent consulting firm who received funding to carry out this analysis.
All other authors have declared no conflicts of interest.

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## P1560 GOOD AND POOR RESPONDERS TO RADIOFREQUENCY ABLATION FOR BARRETT'S OESOPHAGUS RELATED DYSPLASIA: CAN WE PREDICT WHO THEY ARE?

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**Introduction:** Radiofrequency ablation can eradicate dysplasia and intestinal metaplasia in patients with dysplastic Barrett's Oesophagus. However, treatment response may be variable.

**Aims & Methods:** This prospective cohort study aims to determine the factors that affect response to radiofrequency ablation for Barrett's Oesophagus with dysplasia in a tertiary metropolian referral centre. All patients with dysplastic Barrett's Oesophagus treated with regular proton pump inhibitor (PPI) twice a day and with radiofrequency ablation (RFA) from Novbember 2008 to February 2016 were identified. These patients were sorted into two groups according to their response to RFA treatment: Good Responders (GR) (defined as eradication of dysplasia and intestinal metaplasia within 3 or less treatment sessions) and Poor Responders (PR) (defined as patients requiring 4 or more treatment sessions). This was then compared with the patients' age, gender, presence of hiatus hernia, hiatus hernia size, circumferential and maximal length of Barrett's Oesophagus based on Prague classification, grade of dysplasia on histology at referral, and presence of oesophagitis on gastroscopy.

**Results:** Of the 118 patients who have received RFA treatment for dysplastic Barrett's Oesophagus, ninety-seven (82%) patients were classified as Good Responders and 21 (18%) patients were classified as Poor Responders. PR have a longer circumferential length of Barrett's Oesophagus compared to GR (mean length of 8.38 cm vs 3.20 cm, respectively; $p < 0.0001$). PR also had a longer maximal length of Barrett's Oesophagus compared to GR (mean length of 9.71 cm vs 5.22 cm, respectively; $p < 0.0001$). There were a higher number of patients with oesophagitis identified on gastroscopy despite regular PPI therapy in the PR group compared to GR group (8 [40%] vs 7 [10%] respectively; $p = 0.004$). Twenty patients (95%) within the PR group had a hiatus hernia compared to 94 (97%) patients in the GR group, $p = 0.548$. The mean size of hiatus hernias in the PR group and GR group were of 3.61 cm vs 3.09 cm respectively; $p = 0.2068$. PR have a higher proportion of high grade dysplasias and a lower proportion of low grade dysplasias at referral compared to GR (11 [52%] vs 42 [44%], $p = 0.8870$ and 7 [33%] vs 38 [40%]; $p = 0.8870$, respectively). Patients' age and gender did not affect treatment response to RFA.

**Conclusion:** In patients with dysplastic Barrett's Oesophagus, factors such as circumferential and maximal length of Barrett's Oesophagus and presence of oesophagitis on gastroscopy despite regular PPI therapy are associated with poorer response to RFA therapy. Presence of hiatus hernia, hiatus hernia size, grade of dysplasia on histology, age and gender did not affect treatment response to RFA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1561 LYMPH NODE METASTASIS RISK IN BARRETT'S ADENOCARCINOMA DEPENDING ON THE DEPTH OF TUMOUR INVASION: SHOULD WE ENLARGE THE CURATIVE CRITERIA FOR ENDOSCOPIC RESECTIONS?

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**Introduction:** The incidence of oesophageal adenocarcinoma has increased greatly in the western world during the recent decades. However, it is still unclear whether endoscopic treatment can be considered curative for adenocarcinomas invading the upper third of the oesophageal submucosa (sm1).

**Objective:** This multicentre retrospective cohort study aims to assess the risk of lymph node metastasis (LNM) according to the tumour invasion depth through the oesophageal mucosa and submucosa to determine whether endoscopic treatment can be considered curative for early stage adenocarcinoma.

**Methods:** All patients undergoing surgery or endoscopic treatment with curative intent for superficial oesophageal adenocarcinomas (T1a/b) developed on Barrett's oesophagus were included.

**Results:** 201 early stage adenocarcinoma (T1a/b), in 182 patients were included. During the follow up 8 (3.9%) patients developed LNM. The TNM stage of these tumours was: 2 T1m1/2 (2/81; 2.5%), 2 sm1 (2/31: 6.4%), 4 sm2/3 (4/30: 13.3%). The two patients with a T1m1/2 that presented LNM had lymphovascular invasion and a R1 resection respectively. The tumour invasion depths of sm1 patients were 10 µm and 100 µm beyond the muscularis mucosae and both had G3, undifferentiated tumours. Among the G1/G2 tumours without lymphovascular invasion, the risk of LNM was respectively 2.3% (1/43) for m1/m2 lesions, 0% (0/29) for m3 lesions, 0% (0/19) for sm1 lesions, 12.5% (2/16) for sm2/3 lesions

| | Number of lesions | G1/G2 | LNM | Lymphovascular invasion | Risk of LNM |
|---|---|---|---|---|---|
| m1/2 | 81 | 49 (MD: 27) | 2 | 6 | 2.5% |
| m3 | 59 | 34 (MD: 22) | 0 | 0 | 0% |
| sm1 | 31 | 22 (MD: 5) | 2 | 0 | 6.4% |
| sm2/3 | 30 | 19 (MD: 2) | 4 | 7 | 13.3% |

Missing data: MD 21 (10.4%) recurrences occurred and were treated endoscopically for 22 of them and 3 patients had to undergo complementary oesophageal surgery. 69 (37.9%) patients required further curative procedures (Radiofrequency ablation, endoscopic mucosal resection, Endoscopic submucosal dissection, radiotherapy, chemotherapy, Argon plasma coagulation) for local recurrences or to remove the remaining Barrett's tissue. Metachronous oesophageal adenocarcinoma was found in 22 (10.9%)patients and 3(1.5%) patients presented a metachronous local recurrence associated with LNM and metastasis, two years after the initial procedure for two patients and 8 years for the third patient. 41 patients presented an oesophageal stenosis after the initial procedure (endoscopy $n = 30$, surgery $n = 11$) which were all managed successfully endoscopically.

**Conclusion:** Endoscopic treatment for low-risk (i.e. G1/G2 tumours without any lymphovascular invasion) oesophageal adenocarcinoma arising from Barrett's oesophagus with a tumour invasion depth strictly below 500 µm in the submucosa can be considered safe and effective. The removal of the remaining Barrett's oesophagus should be considered as a therapeutic goal, and patients should all go through a strict and lifelong endoscopic surveillance program in order to detect and treat early stage local recurrences.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1562 REDUCING PATIENT'S BURDEN. A MINIMALISTIC APPROACH TO RADIOFREQUENCY ABLATION IN BARRETT'S EPITHELIUM ACHIEVING COMPLETE ERADICATION

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**Introduction:** Radiofrequency ablation (RFA) is an effective and accepted method for the eradication of Barrett's oesophagus. Guidelines advise eradicating high-grade dysplasia (HGD) and/or residual Barrett's after complete endoscopic resection of an intramucosal cancer. After primary circumferential ablation using the HALO$^{360}$ balloon catheter, a subsequent focal RFA session is advised at follow-up to eradicate residual Barrett's but also to routinely perform an additional ablation of the neo-Z-line, irrespective of its endoscopic appearance. The rationale behind this is that often there is insufficient contact between the balloon-based electrode and the mucosa at this level. The aim of this study is to evaluate whether taking biopsies of the neo-Z-line to prove complete eradication of the intestinal metaplasia (CE-IM) and/or dysplasia (CE-D) after the primary ablation, can reduce the number of subsequent ablations of the neo-Z-line.

**Aims & Methods:** All Barrett's oesophagus patients undergoing circumferential RFA (HALO$^{360}$) at a single tertiary center were prospectively registered. After 3 months, eradication of the Barrett's epithelium was evaluated endoscopically. 4-quadrant biopsies were taken just below the neo-Z-line in all patients with complete endoscopic eradication (CEE) of the Barrett segment or when the neo-Z-line was completely eradicated but residual Barrett's more proximal remained. Primary outcome measures were the number of patients with CEE, CE-IM and CE-D, and subsequently how many additional ablation sessions were prevented.

**Results:** 24 patients underwent RFA (HALO$^{360}$) between January 2012 and December 2014. In 19 patients (79%) an endoscopic mucosal resection (EMR) was performed prior to RFA. 15 patients (62%) had CEE of the neo-Z-line after a single RFA session and in 13 patients (54%) biopsies were taken just below the neo-Z-line. Biopsy results demonstrated intestinal metaplasia (IM) with dysplasia in 1 patient (4%), IM but CE-D in 4 patients (17%), and CE-IM in 8 patients (33%). After a mean follow-up of 19 months (range 8–32 months), 7 patients (29%) had persistent CE-IM. Three of these patients underwent additional treatment of proximal residual Barrett's islands by EMR or RFA, and one patient underwent an EMR at the gastro-oesophageal junction for suspicion of buried Barrett's, but pathologically this was not confirmed.

**Conclusion:** This study demonstrates that it is clinically relevant to take biopsies of the neo-Z-line after primary circumferential ablation (HALO$^{360}$) when complete endoscopic eradication of Barrett's oesophagus is observed. In at least 29% of patients, additional ablation of the neo-Z-line can be omitted, which has a significant impact on patient burden, stricture risk and treatment associated costs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1563 TEMPORAL TRENDS OF CLINICAL CHARACTERISTICS OF BARRETT'S ESOPHAGUS IN RECENT TEN YEARS IN SOUTH CHINA

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**Introduction:** Recent studies have reported that the incidence of esophageal adenocarcinoma (EA) in the west had become the fastest rising cancer, which is higher than esophageal squamous cell carcinoma (ESCC) [1–4]. Clinical data of the invasive esophageal cancer cases diagnosed between 1998 and 2003 (n = 65.926) which cover 83% of the US population, collected by the National Program of Cancer Registries or the Surveillance, Epidemiology, and End Results program, showed that the average incidence of ESCC fell by 3.6% yearly whereas the EA increased by 2.1% yearly. The trend of ESCC decreased in both genders and most of the racial or ethnic groups, whereas the EA occurred more in the white or non-Hispanic men [2]. Except for white or non-Hispanic men, ESCC rates were similar to, or greater than, adenocarcinoma rates for men and women of all other races and ethnicities. The largest decrease in ESCC rates occurred in the West census region, which also exhibited no increase in EA rates. The rate of regional and distant-staged EA increased, while rates for local-staged EA remained stable [2]. BE is defined as an oesophagus in which any portion of the normal distal squamous epithelial lining has been replaced by metaplastic columnar epithelium, which is clearly visible endoscopically ($\geq$ 1 cm) above the GOJ and confirmed histopathologically from oesophageal biopsies [5]. The incidence of BE was increased very fast all around the world [1–2]. In the West, BE is considered the major risk factor for EA deterioration and one of the most important precancerous lesion of EA [3]. Studies showed that 2% to 5% of BE could be developed to EA which was 30 to 150 times that of normal people [3]. The prognosis of EA was extremely bad and the 5-year survival rate was only 13% to 15% [1]. The process from BE to EA is a long interval of time and steps, which consists of intestinal metaplasia, low-grade dysplasia, high-grade dysplasia, carcinoma in situ, adenocarcinoma infiltrating. Therefore, early detection and treatment for BE is an important way to prevent EA. In order to provide the evidence of early detection and intervention of BE in China, present study was aimed to evaluate the clinical and endoscopic characteristics of BE.

**Aims & Methods:** The study aimed at evaluating the trend of clinical characteristics of BE in Guangdong area in recent 10 years. Clinical data of 612 patients with BE diagnosed by endoscopy in Guangdong General Hospital from Jan. 2005 to Dec. 2014 were collected and analyzed. The patients were divided into two groups from Jan. 2005 to Dec. 2009 and Jan. 2010 to Dec. 2014.

**Results:** The detection rate of BE was 0.7% (612/87805) in general, which showed an increasing trend from 0.32% in 2005 to 1.29% in 2014. When compared with that in the anterior 5 years, the detection rate of BE in the posterior 5 years rised obviously (0.4% VS 1.0%, p = 0.04). Pathologically, intestinal metaplasia was detected in 13.8% of BE, and there was a significant difference between the two periods (15.1% VS 10.5%, p < 0.04).

**Conclusion:** The detection rate of BE under gastroscopy rises from 2005 to 2014, which may reflect the rising incidence of BE in Guangdong area. The constituent ratio of intestinal metaplasia type of BE is growing, which supports the viewpoint that intestinal metaplasia is the precancerous lesion of esophageal adenocarcinoma.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1564 DEDICATED BARRETT'S OESOPHAGUS SURVEILLANCE LISTS IMPROVES DIAGNOSIS AND DOCUMENTATION OF FINDINGS

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**Introduction:** Oesophageal cancer is the fifth commonest cause of cancer death in the UK, and the incidence of adenocarcinoma is rising. Patients are often without symptoms until the tumour has grown to be inoperable, and the survival for this cancer remains poor. Early diagnosis is crucial to improve survival. Barrett's oesophagus is the pre- cancerous lesion. The British Society of Gastroenterology (BSG) recommends regular surveillance depending on endoscopic and histological findings in order to identify oesophageal cancers at an earlier stage, therefore reducing mortality. There is evidence from previous studies on Barrett's highlighting poor adherence to surveillance intervals, documentation of Barrett's length as well as biopsy protocol. Pooling of Barrett's patients on dedicated Barrett's lists may help with better adherence to guidelines and may enhance detection of dysplasia with better outcomes for patients.

**Aims & Methods:** We aimed to investigate whether a 'dedicated' Barrett's surveillance list improved diagnosis and adherence to the BSG guidelines compared to more 'ad-hoc' surveillance on routine lists. Method: This retrospective study analysed all patients undergoing endoscopy for Barrett's surveillance at a North London hospital over a one-year period. We looked at documentation of the Prague Classification; adherence to the Seattle Protocol; exclusion of Barrett's; biopsy results; and follow up.

**Results:** 76 patients underwent surveillance, with 42 (55%) being performed during the 7 dedicated lists. The dedicated list excluded Barrett's at endoscopy in 7 cases (9.2%) compared to only 1 (1.3%) in the routine list. Documentation was also significantly better with 85% of patients having the Prague Classification recorded, compared to only 32% in the routine group (p < 0.001). Also notable are the 7 patients in the routine group that had missing or erroneous information relating to the Seattle protocol. Adherence to the Seattle protocol was equally poor in both groups (dedicated = 49%, routine = 58%). There was no difference in histology results between the 2 groups. The follow up showed no correlation with the initial list, and frequently didn't adhere to the BSG guidance.

**Conclusion:** We provide evidence that dedicated lists improve both diagnosis and documentation in patients attending for Barrett's surveillance. However, there still appears to be considerable scope for improving adherence to biopsy protocols and follow up plans. The proven benefit of dedicated endoscopic lists could be extended to dedicated follow up clinics to better subsequent management. Despite the stated shortcomings we recommend trials of dedicated lists on a wider scale to investigate whether this has a definite improvement in patient experience and management.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1565 CLINICAL FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH MINIMUM LATERAL MARGIN OF SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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**Introduction:** Endoscopic submucosal dissection (ESD) is an accepted modality for superficial esophageal squamous cell carcinoma (SESCC) leading to en bloc resections and the ability to achieve R0 resection. Esophageal stricture following ESD has been associated with wide mucosal defects greater than three quarter of the luminal circumference[1]. Oral prednisolone or locoregional steroid injections have shown promising results for the prevention of esophageal stricture following ESD[2–3] although some patients developed dysphagia and required repeated endoscopic balloon dilation even after steroid therapies. As iodine staining clearly visualized the margin of SESCC, we applied a border with energy devices and commenced the incision just outside the applied marks to minimize the excision size for large SESCC. This retrospective study aimed to clarify clinical feasibility of ESD with minimum lateral margin of SESCC.

**Aims & Methods:** During 2005 and 2013, 268 consecutive patients with 289 SESCCs underwent ESD at our institution. Of these, 198 patients who underwent endoscopic clearance for initial SESCC and were followed up without any additional treatment were included for analysis. In this study, endoscopic clearance was defined as en bloc resection of SESCC histologically confined to epithelium (EP), lamina propria mucosa (LPM) or muscularis mucosa (MM) without lympovascular invasion and with free vertical margin regardless of the lateral margin. R0 resection was defined as en bloc resection with histologically free lateral and vertical margins. This study excluded 62 patients who didn't meet the criteria of endoscopic clearance and 8 patients who underwent any additional treatment. The majority of patients underwent EGD surveillance on an annual or biannual basis. In addition, computed tomography was performed every 6 months or 1 year to identify lymph node and distant metastases in patients with MM invasion. This study evaluated short- and long-term outcomes including local recurrence in patients with SESCC undergoing endoscopic clearance.

**Results:** Of 198 patients underwent endoscopic clearance with ESD, 137 (69.2%) and 61 (30.8%) patients were classified into R0 and non-R0 group, respectively. Patients and lesions characteristics in both groups were as follows (R0: non-R0): median age (years, (range)) = 67(37–86):70(40–83), male/female = 115/22:52/9, lesion location (Upper/Middle/Lower/) = 10/84/43:5/33/23, the median tumor size (mm, (range)), 23(5–60):30(12–85) (P < 0.01), invasion depth (EP/LPM/MM) = 27/90/20:4/44/13, rates of the mucosal defects greater than three quarter of the luminal circumference = 13.9%(16/137):70.4%(42/61) (P < 0.01), the stricture rates = 11.7%(16/137):19.7%(12/61) (P = 0.14). The median follow-up periods were 3.2 years and 3.9 years in R0 and non-R0 group, respectively. There was no local or nodal recurrence in any group. Cumulative incidence of metachronous SESCC at 3-year is 19.0% and 17.5% in R0 and non-R0 group, respectively (P = 0.63). One patient died of metachronous SESCC in R0 group and none died of esophageal cancer in non-R0 group. The 3-year overall survival rates were 99.1% and 98.3% in in R0 group and non-R0 group, respectively (P = 0.89).

**Conclusion:** ESD for SESCC with minimum lateral margins with our institutions' strategy was oncologically acceptable and this approach could minimize the extent of the resection defect and potentially reduce esophageal stricture after ESD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1566 KI-67 AND P53 IMMUNOHISTOCHEMISTRY AS AN OBJECTIVE DIAGNOSTIC TOOL FOR MANAGEMENT OF INTRAMUCOSAL TUMOR IN BARRETT'S ESOPHAGUS


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**Introduction:** Histological assessment of intramucosal tumors in Barrett's esophagus is important for appropriate therapeutic strategy. In general, high-grade dysplasia, which is nearly identical to intramucosal adenocarcinoma in Japan, and adenocarcinoma are recommended to be treated immediately. However, diagnostic criteria remain subjective, and reproducibility is a big problem.
**Aims & Methods:** The present study aimed to clarify the potential of Ki-67 and p53 immunohistochemistry as an objective criterion by comparing intramucosal cancer with submucosal invasive cancer. Totally 39 superficial Barrett's esophageal adenocarcinoma (24 mucosal cancers and 15 submucosal cancers) in 38 cases, diagnosed by Japanese expert pathologists and resected by endoscopic submucosal dissection (ESD) of surgery between January 2013 to December 2014, were enrolled to this study. Immunohistochemistry for Ki-67 and p53 was performed to each representative section. Ki-67 staining pattern was categorized into two groups: diffuse pattern (positive cells showed diffuse distribution including the surface epithelium) or localized pattern (positive cells were localized to the lower two-third of the crypts). p53 staining was categorized into two groups: normal (wild type) or abnormal (overexpression or loss). Evaluation was performed in intramucosal cancers (Group M), mucosal component of submucosal invasive cancers (Group SM-m), and submucosal component of submucosal invasive cancers (Group SM-sm).
**Results:** Poorly differentiated components were frequently observed in Group SM-sm (73%) compared with Group M and Group SM-m (17% and 40%, respectively). Ki-67 diffuse pattern was more frequent than localized pattern in mucosal cancers (67% and 33%, respectively), whereas all of the submucosal cancers showed diffuse pattern. Abnormal expression of p53 was frequent in all groups (Group M: 83%, Group SM-m: 67%, Group SM-sm: 67%). All of the 8 lesions with Ki-67 localized pattern were intramucosal well-differentiated adenocarcinoma without lymphovascular invasion or lymph node metastasis, despite the high rate of p53 abnormality (6/8, 75%).
**Conclusion:** Majority of intramucosal cancers had identical characteristics to submucosal invasive cancers in terms of Ki-67 and p53 expression patterns. These intramucosal cancers may have invasive potential and therefore have indication for immediate treatment. Immunohistochemistry can be an objective criterion for management of intramucosal tumors in Barrett's esophagus.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1567 PROGNOSIS AND TREATMENT AFTER RECURRENT ESOPHAGEAL CANCER FOLLOWING R0 ESOPHAGECTOMY


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**Introduction:** Esophageal cancer is a highly aggressive malignancy with a high rate of recurrence even after R0 resection.
**Aims & Methods:** The aim of this study was to identify prognostic factors associated with survival of patients with recurrence after R0 esophagectomy for esophageal cancer. A prospective database identified 328 patients who underwent R0 esophagectomy for esophageal squamous cell carcinoma in Kurume University Hospital between January 2000 and December 2014. Of these, 105 patients (32%) developed recurrence. Univariate and multivarite cox regression analyses were used to determine the factors affecting survival after recurrence. Post-recurrence survival was defined as the time between the first recurrence and death or last follow-up.
**Results:** There were 101 males and 4 females, with a median age of 64 years (44–81). Of these, 24 patients (23%) had pT1 tumor, 14 (13%) had pT2 tumor, and 67 (64%) had pT3 tumor. Median time to recurrence was 10.2 months (range 1–49) and 102 patients (97%) developed recurrence within 3 years after surgery. Patients with pT3 cancer developed recurrence earlier than those with pT1–2 cancer (10 months vs 16 months, $P = 0.0006$). Distant recurrence occurred in 71 patients (68%) including 13 patients with both distant and locoregional recurrence, and 34 patients (32%) had locoregional recurrence only. Thirty-five patients (33%) had a single site of recurrence, and 70 patients (67%) had two or more recurrence site. Ninety-one patients (87%) received anticancer treatment; chemoradiotherapy was employed in 38 patients, chemotherapy in 30 patients, radiotherapy in 7 patients, and surgery in 16 patients (including 14 patients with chemotherapy and/or radiotherapy). Fourteen patients (13%) received best supportive care alone. Median post-recurrence survival was 10.4 months (range 1–140), and the overall 1- and 3- year survival rates were 48 and 19%, respectively. Type of recurrence (local vs distant), number of locations (single vs multiple), treatment (anti-cancer vs BSC), and pT at the time of esophagectomy were significantly associated with post-recurrence survival in univariate analysis. Age ( $< 65$ vs $\geq 65$), gender, nodal status (pN0–1 vs pN2–3), and histologic grade (well vs mode or poor) did not affect the survival. In multivariate analysis, type of recurrence (HR 0.561, 95% CI 0.322–0.948; $P = 0.0305$), treatment (HR 0.485, 95% CI 0.264–0.952; $P = 0.0362$), and pT (HR 0.561, 95% CI 0.333–0.924; $P = 0.0229$) were identified as independent prognostic factors associated with post-recurrence survival.
**Conclusion:** In patients with recurrence after R0 resection for esophageal squamous cell carcinoma, distant recurrence, advanced pT stage, and no anticancer treatment were independent prognostic factors associated with worse post-recurrence survival. Although survival after recurrence was poor, treatment could prolong survival and could lead to cure in selected patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1568 OUTCOMES OF SM INVASIVE BARRETT'S CANCERS FOLLOWING ENDOSCOPIC RESECTION: RADICAL INTERVENTION IS NOT ALWAYS REQUIRED?


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**Introduction:** Endoscopic resection (ER) of Barrett's cancer with curative intent is extremely effective for lesions limited to the mucosal layer of the oesophagus. Lesions extending beyond the muscularis mucosae into the submucosa are considered for radical therapy due to risk of lymph node metastases. Radical treatment is not without risk, reported mortality of oesophagectomy is 2–5%.
**Aims & Methods:** All patients referred for ER of Barrett's cancer had data collected prospectively between 2006 and 2015. The database was interrogated by independent researchers blinded to the endoscopic procedures for patients with SM invasive cancers.
**Results:** 261 endoscopic resections were performed in 182 patients during the study period. 26 (14%) patients were identified as having SM invasion following endoscopic resection. 12 had undergone endoscopic submucosal dissection (ESD) and 14 endoscopic mucosal resection (EMR). 22 (85%) lesions were superficially submucosally invasive (SM1), 4 were > SM1 (15%). Table 1 shows outcomes after endoscopic resection. Mean disease free survival was 4.31 years (Range 0.7 to 10.8) in this cohort. 3 patients died of recurrent cancer, 3 patients died of co-morbid conditions.

| | SM1 | >SM1 | Presence of LVI* | Poor Differentiation | Clear of Cancer at follow up |
|---|---|---|---|---|---|
| Endoscopic follow up n = 9 | 9 | 0 | 2 | 1 | 9 |
| Surgery n = 6 | 5 | 1 | 2 | 2 | 5 |
| Chemoradiotherapy n = 7 | 5 | 2 | 2 | 5 | 6 |
| No Intervention n = 4 | 3 | 1 | 0 | 3 | n/a |

*LVI: Lymphovascular Invasion All 9 patients in the endoscopy group were clear of cancer at follow up. There was 1 recurrence that was treated with further ER. Of the 6 patients undergoing surgery 5 had no residual neoplasia in the oesophagectomy specimen (pTxN0M0). 1 patient had a pT1N0M0 cancer with LVI and signet ring cells and died 2 years after surgery. 1 patient was considered for surgery but was turned down due to comorbidities and subsequently died of cancer 6 years following endoscopic resection. 3 patients have been discharged to their referring centres for consideration of surgery. 7 patients underwent chemoradiotherapy. 6 of the 7 patients treated with chemoradiotherapy were clear of recurrence on follow up. 1 patient developed recurrence of cancer and died 2 years after ER.

**Conclusion:** This data further challenges the current paradigm of radical therapy following ER of SM1 Barrett's cancers. Outcomes for patients managed endoscopically are excellent. 5 patients undergoing surgery in our cohort had no residual disease in the oesophagectomy specimen and potentially could have undergone endoscopic follow up alone. Patients found to have SM1 lesions without poor prognostic features can effectively be managed without radical intervention. SM invasive cancers require an individualised management plan tailored to histology and co-morbidities. There does not appear to be a demonstrable difference between chemoradiotherapy and surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1569 TOPICAL MITOMYCIN C TREATMENT FOR RELIEVING ESOPHAGEAL RADIATION-INDUCED STENOSIS

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**Introduction:** Radiation-induced stenosis is common after esophageal cancer treatment, especially at proximal esophagus. Instead of stent placement, endoscopic dilation combined with topical mitomycin C treatment has been reported to improve benign esophageal dysphagia. This study was designed to evaluate the safety and efficacy of this strategy for radiation-induced stricture.

**Aims & Methods:** Patients with esophageal strictures were divided into 2 groups, including dilation in association with mitomycin C injection (mitomycin C group) and dilation in association with saline injection (dilation group). Patients' age, sex, type of stricture, stricture location, number of previous dilations, diameters before and after dilation, and dysphagia-free period were compared.

**Results:** A total of 17 patients were enrolled into this study, including 7 in mitomycin C group and 10 in dilation group. There were no significant difference in baseline characteristics of patients, such as age, sex, type of stricture, stricture location, and number of previous dilations. The major complication was one patient in mitomycin C group with perforation ($P < 0.05$). The minor complications were reported for 4 in mitomycin C group, and 6 in dilation group ($P > 0.05$). The mean dysphagia-free period was $6.33 \pm 1.48$ months in the mitomycin C group, and $3.26 \pm 1.13$ months in the dilation group ($P < 0.05$).

**Conclusion:** Endoscopic dilation combined with topical mitomycin C therapy could prolong the esophageal dysphagia-free period and reduce the frequency of endoscopic dilation, which would be the potential strategy for refractory esophageal stricture.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1570 RADIOFREQUENCY ABLATION (RFA) IN PATIENTS WITH BARRETT'S ESOPHAGUS RELATED NEOPLASIA – LONG-TERM OUTCOMES OF THE CZECH NATIONAL RFA DATABASE

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**Introduction:** Radiofrequency ablation (RFA) with or without endoscopic resection (ER) is a standard endoscopic treatment of early Barrett's esophagus related neoplasia (BORN). We analyzed prospectively collected data from a Czech national database that follows the outcomes of patients with BORN, which have undergone treatment with RFA.

**Aims & Methods:** We collected data from 4 centers (Prague 2x, Ostrava and Olomouc), which perform RFA in the Czech Republic. A total of 170 patients underwent RFA for BORN from April 2009 to April 2016 and 136 patients (115 males, mean age 64), who have already completed the endoscopic treatment, were included into the analysis. Fifty-six patients (41%) were diagnosed with low-grade dysplasia (LGD), 46 (34%) patients with high-grade dysplasia (HGD) and 34 (25%) with early adenocarcinoma (EAC). Mean length of the Barrett's esophagus (BE) segments was 4.5 cm (range 1–13 cm). In 65 patients (48%), RFA was combined with ER or endoscopic submucosal dissection of all visible lesions. After treatment, the patients have undergone regular endoscopic surveillance with multiple biopsies (neo-Z-line and esophagus).

**Results:** Complete remission of IM (CR-IM) and complete remission of neoplasia (CR-N) were achieved in 72.8% (95% CI 64.5–80.1%) and 98.5% (95% CI 94.8–99.8%), respectively. Among 37 patients without CR-IM (27%), 29 (78%) did not have macroscopic signs of BE. During the follow-up, there were 21 recurrences (21%, 21/98 pts) of IM and all of them occurred at the level of neo-Z-line. In 13 of these patients (62%), there were no signs of macroscopic recurrence of BE. Six patients (5%, 6/133 pts) had recurrent neoplasia (5x LGD, 1x HGD). All patients with macroscopic recurrence of BE (8 pts) or dysplasia (6 pts) underwent successful endoscopic re-treatment except for one patient with persistent LGD at the macroscopically normal neo-Z-line who entered endoscopic surveillance. In a multivariate logistic regression analysis, the diagnosis of cancer was an independent risk factor for persistent IM after RFA (p-value = 0.038), but persistent IM at the level of macroscopically normal neo-Z-line was not a risk factor for BORN recurrence. We have not detected buried glands beneath the neosquamous epithelium in any patient. We noticed treatment-related adverse events in 23 patients (17%): 13x chest pain, 8x stricture, 1 x injury of tongue and 1x submucosal tear after balloon calibration. One patient experienced a perforation during balloon dilatation of a post-RFA fibrous stricture and he underwent esophagectomy. All the remaining strictures were managed successfully endoscopically.

**Conclusion:** Radiofrequency ablation is effective in achieving remission of Barrett's esophagus related neoplasia. The recurrence rate of IM/neoplasia was not negligible and patients after successful RFA for BORN still need endoscopic surveillance. Diagnosis of cancer is a risk factor for persistent IM after RFA.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1571 EPIDEMIOLOGY OF ESOPHAGEAL ADENOCARCINOMA IN THE CZECH REPUBLIC. ARE WE AT THE BREAKPOINT OF INCIDENCE?

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**Introduction:** Incidence of esophageal adenocarcinoma (EAC) has increased substantially in developed countries during the past decades. Majority of cases are believed to arise from intestinal metaplasia – Barrett's esophagus, the condition strongly associated with long-term gastroesophageal reflux disease. No data describing epidemiology of histological subtypes of esophageal cancer has been published in the Czech Republic yet.

**Aims & Methods:** Aim of the study was to analyze trends of incidence of esophageal cancer in view of histological types in the Czech Republic. Data from National Cancer Registry regarding esophageal cancer were analysed according to histological main types – adenocarcinoma (EAC), squamous and other types. The changes in incidence during last 30 years were described.

**Results:** Population-based reliable data from National Cancer Registry including histological characteristic are available from years 1984–2013. Adjusted incidence of esophageal cancer generally doubled from 1.7 per 100 000 in years 1984–1988 to 3.16 in years 2009–2013. Adjusted incidence of EAC increased almost four-fold from 0.32 per 100 000 to 1.26 per 100 000 in the same period. Incidence of EAC was about seven-fold higher in men than in women without significant changes in time. Squamous carcinoma was still predominant: 73% in year 1984, 62% in year 2000 and 57% in 2013. The proportion of EAC was increasing from: 18% in 1984, 30% in 2000 and 38% in 2013. We observed a"breakpoint" in the incidence of EAC during the last years. From year 2010 the number of new cases of EAC is rising very slowly.

**Conclusion:** Incidence of EAC in the Czech Republic increased four-fold during last 30 years. Adenoncarcinomas represent still less than half from all oesophageal cancers and its increase is relatively slower in the last years. A broad use of potent drugs for gastroesophageal reflux treatment – proton pump inhibitors during last 20 years may be responsible for slower increase of EAC recently.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1572 ENDOSCOPIC PASSAGE IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA TREATED WITH SURGERY OR CONCURRENT CHEMORADIOTHERAPY: IS IT AN IMPORTANT PROGNOSTIC FACTOR?

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**Introduction:** Surgery and concurrent chemoradiotherapy are widely accepted alternatives for the curative treatment of patients with early stage or locally advanced esophageal cancer. Impossible endoscopic passage due to resistance is intermittently experienced in esophageal cancer patients. The objective of this study was to evaluate the prognostic influence of endoscopic passage in early stage or locally advanced esophageal squamous cell carcinoma patients treated with surgery or concurrent chemoradiotherapy.

**Aims & Methods:** This retrospective case-control study was based on medical records from a single tertiary medical center located in Daejeon, Republic of Korea. The records of 317 patients with esophageal squamous cell carcinoma treated with surgery or concurrent chemoradiotherapy between January 2009 and December 2015 were reviewed, and 160 patients were ultimately selected. These 160 patients were divided into two groups based on their endoscopic passage findings: group A (possible endoscopic passage group), and group B (impossible endoscopic passage group, including patients requiring a pediatric endoscope for passage due to resistance). We then compared the clinical and endoscopic characteristics of these two groups retrospectively.

**Results:** Of the 160 enrolled patients, 92 (57.5%) patients were assigned to group A and 68 (42.5%) to group B. Early stage esophageal squamous cell carcinoma (stage I, II) was significantly more prevalent in group A than in group B patients ($P < 0.05$), and endoscopic stents were less frequently required in group A than

in group B patients ($P < 0.05$). Overall survival was better in group A than in group B patients (85.5% vs 41.4%, $P < 0.05$). Progression-free survival was better in group A than in group B patients (52.3% vs 20.7%, $P < 0.05$). Especially, Similar results came out, even if only patients who underwent concurrent chemoradiotherapy ($n = 92$) have analyzed. Of the 92 enrolled patients, 58 (63%) patients were assigned to group A and 34 (37%) to group B. Overall survival was better in group A than in group B patients (83.8% vs 40.9%, $P < 0.05$), and progression-free survival was better in group A than in group B patients (48.3% vs 23.7%, $P < 0.05$).

**Conclusion:** Our data suggest that endoscopic passage was an important prognostic factor in terms of overall survival and progression-free survival in patients with early stage or locally advanced esophageal squamous cell carcinoma treated with surgery or concurrent chemoradiotherapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1573 PREVALENCE OF GASTRIC ATROPHY AND INTESTINAL METAPLASIA AMONG PATIENTS WITH GASTRIC AND DUODENAL ULCERS IN SAXONY-ANHALT, A REGION AT INCREASED RISK FOR GASTRIC CANCER


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**Introduction:** *Helicobacter pylori*-induced gastric atrophy (GA) and intestinal metaplasia (IM) are risk factors for gastric ulcer (GU) and intestinal-type gastric cancer (GC).

**Aims & Methods:** We aimed to determine the prevalence of GA and IM in patients with GU and duodenal ulcer (DU) in a tertiary hospital of Saxony-Anhalt, Germany, a region at increased risk for gastric cancer. Methods. Histology based on at least 4 gastric biopsies was available in 1073 (62.3%) out of the 1722 patients (male 60%, mean age 65.7 years) with endoscopic GU and DU diagnosed by January 1st 2004 to December 31st 2014. Demographics, intake of aspirin/non-steroidal anti-inflammatory drugs (NSAIDs), and ulcer localization were documented. Patients with positive results for at least one assay among histology, 13C-urease breath test, rapid urease test or serology were considered *H. pylori*-positive.

**Results:** Overall, 47.3% of patients had GU, 42.2% had DU and 10.5% had ulcers in both localisations. The prevalence of *H. pylori* infection, aspirin/NSAID intake and the presence of both risk factors was 35.1%, 38.7% and 13.0% respectively. Prevalence of extensive GA/IM (excluding mild/moderate GA/IM confined to the antrum) was significantly higher in patients with GU compared to DU (20.3% vs. 6.4%, respectively, $p < 0.0001$). Patients with ulcers of the gastric corpus/fundus were more likely to have extensive GA/IM compared to those with ulcers located in the gastric antrum/duodenum (OR 2.83; 95% CI: 1.868- 4.285). The prevalence of mild GA/IM was higher among patients with *H. pylori* infection compared to non-infected patients (20.5% vs. 12.5%, $p < 0.0001$), whereas the prevalence of extensive GA/IM was independent of *H. pylori* infection (13.3% vs. 14.3%). Prevalence of GA/IM of any grading did not differ between patients with and without aspirin/NSAID intake (30.1% vs. 29.6%), independently from ulcer location.

**Conclusion:** The high prevalence of GA/IM in patients with GU may account for the increased risk of intestinal-type GC in this population. The more proximal the ulcer location, the higher was the likelihood of having GA/IM. After early exclusion of a malignant ulcer, follow-up endoscopy should be offered to patients with GU and extensive GA/IM.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1574 PANTOPRAZOLE DOES NOT INFLUENCE THE ANTIPLATELET EFFECT OF CLOPIDOGREL: A RANDOMIZED CONTROLLED TRIAL


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**Introduction:** Proton-pump inhibitors (PPIs) are often prescribed in combination with thienopyridines. Conflicting results exist as to whether PPIs diminish the efficacy of clopidogrel (1–3).

**Aims & Methods:** We sought to evaluate the influence of pantoprazole, indicated as relatively less influent than other PPIs, on the antiplatelet effect of clopidogrel, considering a stratification of the population for the presence of cytochrome (CYP) 2 C19 polymorphism. Forty patients who received dual antiplatelet therapy, were randomized between pantoprazole ($n = 20$) or ranitidine ($n = 20$). The platelet aggregation was evaluated by impedance aggregometry (in Ohm) induced by with 5 $\mu$M adenosin diphosphate (ADP), on baseline (D0) and 8 days after acid-lowering treatments (D9). CYP2C19 was genotyped by polymerase chain reaction–restriction fragment length polymorphism.

**Results:** Demographic, clinical and procedural data and the prevalence of CYP2C19 polymorphism were similar between the two groups. After co-treatment, the percentage of clopidogrel low-response (CLR) was 11.1% (2/18) in the pantoprazole group and 10.5% (2/19) in the ranitidine group ($P = 0.954$). Not statistically differences were observed for the values of impedance with ADP stimulus after acid-lowering treatments. At the multiple regression analysis, only event of ST-elevation myocardial infarction was marginally associated with a reduced antiplatelet effect (OR: 12.07, 95% CI: 0.84–173.78). However, pantoprazole use did not affect the antiplatelet effect considering of CYP2C19 polymorphism.

**Conclusion:** This randomized trial showed pantoprazole does not increase platelet aggregation in patients treated with dual antiplatelet therapy after correction for the bias of CYP2C19 polymorphism.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1575 CHRONIC ATROPHIC GASTRITIS IN ITALY: A POPULATION STUDY ON 10,000 PEOPLE


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**Introduction:** Chronic atrophic gastritis (CAG) represents a stomach precancerous condition often related with *Helicobacter pylori* (H.p.) infection. This feature is characterized by hypo- achloridria due to loss of appropriate gastric glands. Gastropanel® is a non-invasive test able to detect both CAG and H.p. infection. This test is defined as a "serological biopsy" pointing out both morphological and functional status of gastric mucosa.

**Aims & Methods:** The aim of the present study is to investigate the frequence of CAG in a study population in primary care setting by means of a non-invasive test.

Ten thousand dyspeptic patients were enrolled from two different areas of North-East of Italy. In the first one –Group A-, 7,400 patients were enrolled (M:F = 1,2:2, mean age 53 years) from 2003 to 2014, in the second one –Group B- 2,600 patients (M:F = 1,5:2,3, mean age 56 years) were enrolled from 2011 to 2013.

Upper GI endoscopy with biopsies sampling according with Sydney classification or O.L.G.A. staging and Gastropanel® (Biohit Oyj, Helsinki, Finland) were performed in every patients.

Serological diagnosis of CAG was assessed by means of a feature of PGI $< 25$ microg/L, G-17 $> 14$ pmol/L; histological diagnosis of CAG following the criteria of both Sydney system and O.L.G.A. staging.

**Results:** Overall, CAG was diagnosed by serology in 716 out of 10.000 patients. In Group A population the diagnosis of CAG was made in 608 patients (mean

age 57 years), in 2,492 a diagnosis of non-atrophic gastritis (N.A.G.) related with H.p. infection was assessed (mean age 54), in 879 patients a normal gastric morpho-functional assessment was described (mean age 44).
In Group B population the diagnosis of CAG was made in 108 patients (mean age 58 years) in 643 a diagnosis of NAG related with H.p. infection was performed (mean age 59), in 721 patients a normal gastric morpho-functional assessment was detected (mean age 47).
**Conclusion:** Overall, a picture of CAG was found in the investigated population in 7.16% out of patients.
In Group A CAG was found in 608 out of 7,400 patients (8.2%), in Group B in 108 out of 2,600 patients (4.15%).
The mean age of subjects with CAG was higher than in patients with NAG H.p related and normal population in both the two areas (Group A: CAG = 57 yrs, NAG h.p. 54 yrs, normal subjects 44 yrs; Group B: CAG 58 yrs, NAG H.p. 59 yrs, normal subject 47 yrs).
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1576 RECOVERY OF GASTRIC FUNCTION IN CHRONIC ATROPHIC GASTRITIS: A 3 YEARS STUDY

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**Introduction:** The relationship between *Helicobacter pylori* (*H. pylori*) eradication and atrophic changes in the gastric mucosa has not yet been fully elucidated. Although some studies report a partial restoration of serum pepsinogen I (PGI) levels after eradication, it is not clear whether this finding reflects gastric mucosal healing on a morphological level. L-cysteine, an agent capable of reducing acetaldehyde production after food intake, has recently been proposed for prevention of gastric carcinogenesis in patients with atrophic gastritis.
**Aims & Methods:** To assess modifications in gastric function after L-cysteine administration in moderate-severe chronic, atrophic, body gastritis by means of PGI, PGII and G-17 serum levels. 17 patients (11 men, mean age 47.2 yrs, range 27–65 yrs), with histological diagnosis of moderate to severe chronic, atrophic, body gastritis (according to the O.L.G.A. staging system) and PGI serum levels < 25 microg/L, underwent upper gastrointestinal endoscopy with gastric biopsy samplings and PGI, PGII and G-17 measurement by means of Gastropanel® (Biohit Oyj, Helsinki, Finland). All patients were *Helicobacter pylori* negative at baseline. 6 out of 17 patients had autoimmune gastritis while 11 of them reported previous H.p. infection. All the patients were treated with L-cysteine (100 mg three times daily) for 36 months. Serum PGI, PGII and G-17 were measured at baseline and after 3, 6, 12, 24, 36 months after starting therapy.
**Results:**

| Patients(n°17) | Basal Value | T_3m | T_6m | T_12m | T_24m | T_36m | p Value |
|---|---|---|---|---|---|---|---|
| PG1(mcg/L, mean) | 8.42 | 10.58 | 11.45 | 12.19 | 13.88 | 14.21 | 0.0001 |
| G17(pg/L, mean) | 51.33 | 43.13 | 38.66 | 34.41 | 28.34 | 26.03 | 0.0041 |

Results are summarized in the Table.
**Conclusion:** After L-cysteine administration, patients with chronic, atrophic, body gastritis showed long-lasting improvements of physiological gastric function, reflected by a significant increase of PGI levels and a parallel decrease of G-17 serum levels over a 36 months follow-up period.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1577 LONG-TERM OUTCOMES OF ENDOSCOPIC RESECTION FOR PAPILLARY ADENOCARCINOMA IN EGC

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**Introduction:** Although papillary adenocarcinoma (PAC) of stomach is classified as a differentiated-type cancer, some studies have reported that it has more aggressive feature than tubular adenocarcinoma. This study aimed to evaluate the outcomes of PAC diagnosed after endoscopic resection for early gastric cancer (EGC).
**Aims & Methods:** PAC was defined when papillary structures were revealed in more than 50% of resected tumor. The therapeutic outcomes were assessed retrospectively in 33 EGCs diagnosed as PAC after endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). The long-term outcomes were evaluated in 19 patients after excluding 14 patients with less than 12 months of follow-up period.
**Results:** Thirty-three PACs were treated with EMR (n = 19, 57.6%) and ESD (n = 14, 42.4%). The mean size of tumors was 23.2 mm, and most of them were located in lower- (n = 18, 54.5%) and mid- (n = 12, 36.4%) third of the stomach. The rates of complete resection and curative resection were 81.8% (78.9% in EMR, 85.7% in ESD) and 78.8% (79.0% in EMR, 78.6% in ESD), respectively. For non-curative resection (n = 7), 3 underwent additional treatment (1ESD, 2 surgical treatment), and 4 were not followed up without additional treatment. No local or distant recurrence occurred after complete resection or additional treatment for non-curative resection during a mean follow-up period of 30.3 months.
**Conclusion:** Endoscopic resection for PAC showed acceptable therapeutic and long-term outcomes. Surveillance can be considered without additional treatment for PAC if the resected lesion shows curative resection that meets the definition of complete resection and the absolute or expanded ESD criteria on the pathological result from endoscopic treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1578 PROPOSAL FOR A NEW AGGRESSIVE VARIANT OF GASTRIC ADENOCARCINOMA OF FUNDIC GLAND TYPE (A MULTICENTER STUDY OF 50 CASES)

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**Introduction:** We previously proposed gastric adenocarcinoma of fundic gland type (chief cell predominant type, GAFG-CCP) as a new form of gastric adenocarcinoma with distinct clinicopathological and endoscopic features ((1) Ueyama H. *Am. J. Surg. Pathol* 2010, (2) Ueyama H. *Endoscopy* 2014, (3) Ueyama H. *Stomach and intestine* 2015). GAFG-CCP 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. With regard to biological behavior, GAFG-CCP is considered less aggressive because it exhibits low cellular atypia, no lymphovascular invasion, low proliferative activity, a lack of p53 protein overexpression, and good prognosis. We also analyzed the molecular events of GAFG, and suggested that a progression of GAFG, at least in part, might be associated with GNAS mutations. Recently, many cases of an aggressive variant of GAFG with high cellular atypia have been discovered. This variant exhibited differentiation toward gastric foveolar epithelium in addition to fundic gland differentiation, and it was designated gastric adenocarcinoma of fundic gland mucosal type (GAFGM). However, the clinicopathological features of GAFGM have not been well investigated.
**Aims & Methods:** The aim of this study was to clarify the clinicopathological features of GAFGM by comparisons with pure GAFG. A total of 50 GAFG cases from January 2008 to December 2015 were retrospectively collected from 24 institutions. We performed an immunohistochemical analysis using 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+, n = 34) or GAFGM (MUC5AC+, ≥10%·MUC6+·pepsinogen-I+, n = 16). We then compared the pure GAFG and GAFGM cases via a clinicopathological evaluation.
**Results:** There were no significant differences between the two groups (pure GAFGs vs. GAFGMs) in the following findings: location of lesion (U/M/L), 31/3/0 vs. 11/4/1; method of treatment (ESD/EMR/OPE), 24/6/4 vs. 9/1/6; depth of invasion (M/SM), 7/27 vs. 2/14; lymph node metastasis, 0/3 vs. 1/9; proliferative activity (mean MIB1-LI, %), 6.1 vs. 8.9; p53 protein overexpression (+/-), 0/34 vs. 2/9; and *H. pylori* infection (positive/negative/after eradication), 3/20/3 vs. 1/7/1. Macroscopically, the depressed type was observed more often in GAFGMs (protruded/flat/depressed type, 22/4/8 vs. 6/0/10, p = 0.07). The size of the tumor (10 ± 7.7 mm vs. 24.2 ± 20 mm, $p < 0.05$) and depth of submucosal invasion (278.9 ± 277.5 $\mu$m vs. 1182.1 ± 1428.2 $\mu$m, $p < 0.05$) 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 (2.9% vs. 37.5%, $p < 0.01$). Immunohistochemically, pure GAFGs presented positivity for pepsinogen-I > MUC6 (70.6%); in contrast, GAFGMs presented positivity for MUC6 > pepsinogen-I (87.5%) ($p < 0.001$). The predominant cell differentiation type in GAFGMs did not differ significantly between fundic gland cells and foveolar epithelial cells. Activating mutations in GNAS were found more frequently in GAFGMs (50%, 3/6) than in GAFGs (9%, 1/11) (p = 0.09).
**Conclusion:** GAFGM should be categorized as a new aggressive variant of GAFG that has high malignant potential, differentiates predominantly toward MUC5AC and MUC6, and might be associated with GNAS mutations.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**Table:** The distribution of gastric lesions within the groups defined by pepsinogen test results

| Criterion | Normal pepsinogens N = 126 | Moderately decreased pepsinogens N = 133 | Severely decreased pepsinogens N = 57 |
|---|---|---|---|
| **Severe corpus atrophy** | 0 | 5 (3.76%; 95% CI 0.53%–6.99%) | 4 (7.02%; 95% CI 0.39% -13.65%) |
| **OLGA III** | 0 | 6 (4.51%; 95% CI 0.98%–8.04%) | 6 (10.53%; 95% CI 2.56%–18.5%) |
| **OLGA IV** | 0 | 0 | 0 |
| **OLGIM III** | 0 | 2 (1.50%; 95% CI 0.57%–3.57%) | 2 (3.51%; 95% CI 0.38%–6.64%) |
| **OLGIM IV** | 0 | 0 | 0 |
| **Dysplasia** | 3 (2.38%; 95% CI 0.28%–5.04%) | 17 (12.78%; 95% CI 7.11%–18.45%) | 9 (15.79%; 95% CI 6.32%–25.26%) |
| **Gastric cancer** | 0 | 2 (1.50%; 95% CI 0.57%–3.57%) | 1 (1.75%; 95% CI 1.65%–5.15%) |
| ***H. pylori* positivity** | 76 (60.32%; 95% CI 51.78%–68.86%) | 95 (71.43%; 95% CI 63.75%–79.11%) | 31 (54.39%; 95% CI 41.46%–67.32%) |

## P1579 THE ELEMENTS THAT MAY CAUSE THE DIFFICULTY TO DIAGNOSE EARLY GASTRIC CANCER AFTER HELICOBACTER PYLORI ERADICATION

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**Introduction:** Narrow band imaging with magnifying endoscopy (NBI-ME) criteria for early gastric cancers (EGC) were based on the microvascular architecture and/or microsurface structure with clear demarcation between the cancerous area and surrounding non-neoplastic area. EGC after successful *Helicobacter pylori* eradication is often difficult to diagnose. Therefore careful observation is required in these cases. One of the elements that makes the diagnosis difficult is the non-neoplastic epithelium which cover the periphery of the cancer and some might exist among the cancer tubules after eradication. This might leads to the unclear demarcation under NBI-ME.

**Aims & Methods:** The aim of this study is to clarify the histopathological characteristics to maximize the accuracy of the diagnosis. This is a retrospective control study. There were 199 cases of EGC performed endoscopic submucosal dissection (ESD) between November 2011 and October 2015 in Okayama Medical Center. We included 19 lesions from 14 patients who had received *H. pylori* eradication in the eradication group. As a control group, 19 lesions from 19 patients who had persistent *H. pylori* infection and had not received eradication in the same period were selected and were matched the background to the eradication group. The specimens after ESD were cut by 2 mm width. The retrospective evaluation of histopathological findings was performed in both groups which includes 74 sections with lesions from eradication group and 79 sections with lesions from control group. We evaluated 1) the rate of sections that contains non-neoplastic epithelium covering the carcinoma, 2) the length of the non-neoplastic epithelium, 3) the rate of sections that non- neoplastic tubules exist among cancer tubules, 4) the ratio of the area where non-neoplastic tubules exist in tumor lesion. In the eradication group, each cancer area of sections were divided equally into 4 parts, 2 central parts as 'center area' and 2 marginal parts as 'marginal area'.

**Results:** The rate of sections that contains non-neoplastic epithelium covering the carcinoma was 63.5% (47/74) in the eradication group, which was significantly higher by 35.4% (28/79) than the control group ($p = 0.009$). The average length of the non-neoplastic epithelium covering the carcinoma was 1.07 mm in the eradication group, and was 0.81 mm in the control group. The rate of sections that non-neoplastic tubules exist among the cancer tubules was 20.3% (15/74) in the eradication group was significantly higher ($p = 0.004$) than the control group (10.1% (8/79)). In the eradication group, the area where non- neoplastic tubules exist among the cancer tubules was 21.1% in center part, 78.9% in marginal part.

**Conclusion:** In the eradication group, both rate of sections that contains non-neoplastic epithelium covering the carcinoma and non-neoplastic tubules exist among the cancer tubules were significantly higher than the control group. And non-neoplastic tubules existed more in the marginal part. Thus, it can be said that these results lead the demarcation becomes unclear in the EGC after eradication.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1580 THE YIELD OF PEPSINOGEN TESTING IN A GENERAL POPULATION SAMPLE OF CAUCASIAN ORIGIN

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**Introduction:** Pepsinogen testing has been suggested to be the best available non-invasive screening tool for atrophy as the precursor of gastric cancer by several international guidelines, including by Kyoto international consensus and Maastricht V. However, studies addressing the yield of this type of screening are originating predominantly from Asia; little evidence is available from general population studies in Caucasians.

**Aims & Methods:** Individuals from a cross-sectional population-based study in Latvia with decreased pepsinogen levels during the recruitment were invited to undergo upper endoscopy with a proper biopsy work up. The results of the initial tests have been described elsewhere[1]. Blood samples were obtained prior to the endoscopy. Pepsinogen I and II was measured in plasma simultaneously from either in the initial or the follow-up sample by a latex-agglutination test system (from Eiken Chemical Co., Tokyo, Japan). Moderately decreased pepsinogen results were considered if PgI≤70 ng/ml and PgI/PgII≤3, but severely decreased if PgI≤30 ng/ml and PgI/PgII≤2; the remaining cases were considered to have normal pepsinogen levels. The presence/absence of the gastric mucosal lesions was scored according to the OLGA and OLGIM staging systems. The presence of *H. pylori* IgG was assessed serologically (Mikrogen Diagnostik, Neuried, Germany).

**Results:** Results from 259 individuals (31.7% men; median age 58 years, range 22–88) were available for the analysis. The median follow-up interval was 3.5 years (range 3–6 years). Two gastric cancer cases (0.8%) and 29 cases with dysplasia (11.2%) were identified. Moderately decreased pepsinogens according to the results from the initial sample collected during the recruitment process was found in 133 subjects (51.4%), severely decreased – in 57 cases (22.1%). The distribution of the precancerous lesions between the groups is given in the Table. No significant further decrease in the pepsinogen values was observed between the initial and follow-up samples.

**Conclusion:** Pepsinogen detection could be a useful tool for identification of subjects at increased risk for developing gastric cancer in general Caucasian population; however only the minority of individuals with decreased pepsinogen levels are presenting with advanced gastric mucosal lesions.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1581 FACTORS THAT ARE ASSOCIATED WITH UPGRADE DIAGNOSIS TO SUBMUCOSA OR LYMPHOVASCULAR INVASIVE EARLY GASTRIC CANCER FROM HIGH GRADE DYSPLASIA

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**Introduction:** Gastric high-grade dysplasia (HGD) is a precancerous lesion. Although Vienna classification recommend endoscopicresection for gastric HGD, 50–70% lesions of resected gastric HGD were diagnosed as gastric cancer. In addition, it is also emerging as a submucosal (SM) cancer or lymphovascular invasion cancer.

**Aims & Methods:** The purpose of the present study is to evaluate predictable factors for pathologic upgrade diagnosis to early gastriccancer (EGC) in patients who HGD diagnosed by endoscopic biopsy and underwent ESD. Additionally, we investigated the risk factors associated with SM cancer or lymphovascular invasion cancer. Between November 2008 and August 2015, a retrospective analysis of a prospective database was conducted at a single tertiary referral center. A total of 295 ESD procedures were carried out for gastric HGD lesions identified by EFB. The rate of being diagnosed with cancer and the predictable factors for upgrade diagnosis to cancer were analyzed.

**Results:** En bloc resection and complete resection rate were 98.6% and 98.9% of the total 295 ESD cases. Pathologic discrepancy between EFB and final resection was 65.8% (194/295). One hundred fifty-two lesions (51.5%) were finally diagnosed EGC (126 mucosal cancers, 26 submucosal cancers, 3 lymphovascular invasion cases) by ESD. Forty two lesions (14.2%) were diagnosed rather downgrade, such as low-grade dysplasia (LGD 37, gastritis 3 and hyperplastic polyp 2). Multivariate analysis revealed that lesion central depression

(OR 3.069 [95% CI 1.528~6.167]), surface redness (OR 2.006 [95% CI 1.011~3.981]) and nodular surface (OR 3.210 [95% CI 1.541~6.688]) were significant risk factors associated with EGC. Additionally, multivariate analysis revealed that only SM fibrosis (OR3.643 [95% CI 1.478~8.981]) was significant risk factor associated with SM cancer or lymphovascular in vasion cancer.
**Conclusion:** Risk factors associated with diagnosed with EGC in HGD patients in the endoscopic biopsy were central depression, surface redness and nodular surface. Futhermore, if you see a SM fibrosis during the ESD procedure SM or lymphovascular invasion cancer probability is higher. Therefore patients with these risk factors should be explained that they may require further surgery in some cases.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1582 WHAT ARE THE FACTORS ASSOCIATED WITH DIFFICULT GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION?

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**Introduction:** Endoscopic submucosal dissection (ESD) is a widely accepted treatment for gastric superficial neoplasm. ESD can lead to serious complications, such as aspiration pneumonia and perforation.
**Aims & Methods:** The aim of this study was to define the difficult ESD and to know the associated factors with difficult ESD. Between January 2012 and September 2014, a total of 1052 ESD procedure were performed at Pusan National University Yangsan Hospital. Difficult ESD was defined by any one of three factors: long procedure time (≥60 minutes), piecemeal resection or occurrence of perforation. To know the associated factors with difficult ESD, clinico-patholgic features and endoscopic findings were analyzed.
**Results:** The rate of difficult ESD was 9.8% (104/1052). Long procedure time (>60 minutes) was 4.8% (51/1052), piecemeal resection was 6.6% (70/1052) and perforation was 0.5% (6/1052). By multivariate analysis, tumor size (≥20 mm) (odds ratio [OR] 2.7; 95% confidence interval [CI] 1.7–4.3), submucosal fibrosis (OR 3.8; 95% CI 2.4–6.1), location of upper third (OR 2.0; 95% CI 1.1–3.8) and submucosal invasion (OR 2.0; 95% CI 1.1–3.8) were associated with difficult ESD.
**Conclusion:** Lesions with size larger than 20 mm, location of upper third, lesions with submucosal fibrosis were associated factors related with difficult ESD. Before performing ESD for lesions which have these risk factors, endoscopists should perform ESD more precisely, and inform the patients about the possible complications.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1583 CLINICAL IMPACT OF OBESITY FOR THE PATIENTS WHO UNDERGO ENDOSCOPIC SUBMUCOSAL DISSECTION

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**Introduction:** Obesity is considered one of the unfavorable factors for perioperative outcomes in gastric cancer patients. This study aimed to investigate the clinical impact of overweight or obesity in the patients who received endoscopic submucosal dissection (ESD) with gastric adenoma or early gastric cancer.
**Aims & Methods:** A total of 1571 consecutive patients with gastric neoplasia who underwent ESD at Seoul St. Mary's hospital between December 2010 and March 2016 were enrolled for the study. We analyzed 1181 cases retrospectively, which were divided into three groups by patient's body mass index (BMI) according to the International Obesity Task Force criteria for the Asia-Pacific population: Normal (BMI $< 23\,kg/m^2$, n = 411), Overweight ($23 \leq BMI < 25\,kg/m^2$, n = 312), and Obesity group ($BMI \geq 25\,kg/m^2$, n = 458). Demographics, endoscopic findings, pathologic results and clinical outcomes were analyzed.
**Results:** No significant differences were observed in failure of procedure, en-bloc resection rate, resection margin involvement, invasion into submucosa, or lymphovascular invasion of tumor cells between three groups. In contrast, men were more overweight or obese, and overweight and obesity patients showed longer procedure time (normal vs. overweight vs. obesity, $42.2 \pm 42.6$ vs. $43.8 \pm 35.6$ vs. $49.8 \pm 46.6$ respectively; $p = 0.001$ by Jonckheere-Terpstra test) and the number of the cases which spent 60 minutes or longer were also different (17.3% vs. 22.4% vs. 25.8% respectively, $p = 0.010$). The three groups did not show significant differences in the complication rates including perforation, early and delayed bleeding and subsequent operation after non-curative ESD. We analyzed the factors in relation with longer procedure time over 60 minutes. In univariate analysis, male ($p < 0.001$), obesity ($p = 0.003$), body lesions in longitudinal axis ($p < 0.001$), lesions of lesser curvature ($p = 0.018$), resected lesion size ($p < 0.001$), cancer pathology ($p < 0.001$), tumor invasion into submucosa ($p < 0.001$), and occurrence of the complications ($p < 0.001$) were significantly associated with the longer operation time. In multivariate analysis, we found that male sex ($p = 0.008$), obesity ($p = 0.007$), higher location of the lesion ($p = 0.000$), submucosal invasion ($p = 0.012$) and occurrence of the complication ($p = 0.001$) were independent factors associated with longer procedure time.
**Conclusion:** These results showed that obesity or overweight was not directly associated with clinical outcomes. However, obesity or overweight influenced longer procedure time. Although gastric ESD might be difficult in the obesity patients, it can be performed safely with sufficient precaution.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1584 ENDOSCOPIC PAPILLECTOMY FOR AMPULLARY ADENOMAS: AN ITALIAN SINGLE CENTRE EXPERIENCE

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**Introduction:** Endoscopic papillectomy (EP) has been recognized as a safe and valuable therapeutic procedure for ampullary adenomas that can obviate the need for potentially major surgical intervention. This study aims to evaluate the effectiveness, the safety and the outcome of this technique.
**Aims & Methods:** In this study we considered all the consecutive patients underwent endoscopic papillectomy because of ampullary tumor at Arcispedale Santa Maria Nuova (Reggio Emilia, Italy) between January 2001 and January 2014. Only patients with diagnosis of ampullary adenoma on the endoscopic resection specimen were included in the analysis. The primary outcome of the study was the technical success of the papillectomy, defined as: a) complete endoscopic removal, even in multiple sessions, confirmed by the absence of residues at histology at the first follow-up; b) endoscopically treated recurrence. Technical failure was defined when at least one of the following criteria was met: a) histology > pT1; b) residual adenomatous tissue not suitable of endoscopic resection; or c) recurrence referred to surgery. The secondary outcomes were the incidence of adverse events, the incidence of recurrence, and the comparison of these outcomes between patients with sporadic ampullary adenomas (SAA) and patients with FAP-associated ones.
**Results:** Among 106 patients with a sospiciuos ampullary tumor, 56 underwent PE for ampullary adenomas: 20 FAP and 36 SAA. Male:38/56 (68%), Median age: 62 ys (20–91); Median size of the lesion: 16 mm (5–80). 49 patients (87.5%) completed at least 24 months follow up. Technical success was achieved in 40 patients (75%): 18 (90%) FAP and 22 (61%) SAA. Mean number of endoscopic session to complete resection was 1.6 (1–4). Recurrence rate (during a 24 month FU) was 7 (12.5%): 3 FAP (15%), 4 SAA (11%); 2 of these (3.5%) were referred to surgery. Morbidity rate was 16.1%, included bleeding in 5 patients (8.9%), and 4 acute pancreatitis (7.1%), all conservatively treated. No perforation or death occurred. Histology showed: nonspecific changes (10.7%), low-grade dysplasia (37.5%), high-grade dysplasia (39.3%) and carcinoma (10.7%). No carcinoma in the FAP group. Biopsy sampling accuracy was higher for low-grade dysplasia (76.2%) compared with high-grade dysplasia (25.0%) or carcinoma (0%) in both group.
**Conclusion:** Endoscopic papillectomy of selected ampullary tumors is a safe and effective procedure and, since it can achieve a complete endoscopic resection, it should be established as the first-line therapy of ampullary adenomas, representing a viable alternative to surgical therapy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1585 THE EFFECTIVENESS AND LONG-TERM OUTCOMES OF CARCINOMATOSIS AND ASCITES STATUS OF PALLIATIVE TREATMENT IN THE PATIENTS OF ADVANCED GASTRIC CANCER WITH BOWEL OBSTRUCTION: STENT PLACEMENT VERSUS PALLIATIVE SURGERY

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**Introduction:** Advanced gastric cancer (AGC) patients with colorectal obstruction usually underwent palliative therapy by using self-expandable metal stent (SEMS) placement or surgery. However, the clinical efficacy and impact of carcinomatosis and ascites status have not been evaluated in patients with colorectal obstruction by AGC according to treatment modalities.
**Aims & Methods:** We retrospectively evaluated 232 patients with colorectal obstruction in AGC that were diagnosed between 2006 and 2014. The study population was analyzed by the patency and overall survival between SEMS placement versus surgery according to carcinomatosis and ascites status.

**Results:** The median age of the study population (126 men, 106 women) was 55 years (SD 12.8). During the follow-up period (mean 24 months, SD 32), 185 (79.7%) patients deployed SEMS and 47 (20.3%) patients received palliative colorectal surgery. The clinical success (57.3% vs 78.7%, P = 0.007) and technical success rate (74.1% vs 93.6%, P = 0.004) were higher in the palliative surgery group than the SEMS placement group. On multivariate analysis, over three lesions of obstruction (HR, 0.237; 95% CI, 0.065–0.860; P = 0.029) and SEMS placement (HR, 0.340; 95% CI, 0.127–0.911; P = 0.032) were independent factor of clinical success. The relative risk of reobstruction was associated with right side of the bowel obstruction (HR, 0.443; 95% CI, 0.211–0.929; P = 0.031), post-chemotherapy (HR, 1.836; 95% CI, 1.006–3.353; P = 0.048), and SEMS placement (HR, 4.022; 95% CI, 1.253–12.913; P = 0.019). The patency of palliative surgery group was longer than the SEMS placement group (P = 0.003 by log-rank test). In subgroup analysis, the patients with good performance who had carcinomatosis with ascites, the patency duration was longer in the surgery group than in the SEMS placement group (P = 0.002 by log-rank test). In patients who had neither carcinomatosis nor ascites, patency duration was longer in the surgery group than in the SEMS placement group (P = 0.041 by log-rank test). In a subgroup of patients who had carcinomatosis without ascites, patency duration was not significantly different between surgery groups and the SEMS placement groups (P = 0.371 by log-rank test). The overall survival rates were not significantly different between surgery and the SEMS placement groups according to carcinomatosis with ascites status.
**Conclusion:** The efficacy of palliative treatment modality for bowel obstruction caused by AGC was affected by carcinomatosis and ascites status.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1586 A NOVEL METHOD OF LAPAROSCOPIC-ENDOSCOPIC COOPERATIVE SURGERY FOR GASTROINTESTINAL STROMAL TUMORS OF THE STOMACH


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**Introduction:** Laparoscopic endoscopic cooperative surgery (LECS) for gastrointestinal stromal tumors (GIST) was developed in 2008 in Japan and enables the dissection of lesions in a less invasive manner. Recently, modified LECS, such as non-exposed endoscopic wall-inversion surgery (NEWS), and the combination of laparoscopic and endoscopic approaches to neoplasia with a non-exposure technique (CLEAN-NET) were introduced to avoid tumor cells seeding into the peritoneal cavity. We describe a novel method of non-exposure LECS (Closed LECS) for GIST of the stomach.
**Aims & Methods:** Between January 2015 and October 2015, a total of four consecutive patients with GIST of the stomach less than 30 mm in diameter were treated by Closed LECS, which was performed as follows: The patient was placed in a supine position under general anesthesia. A 12 mm camera port was inserted into the umbilicus, and then 5 mm trocars were placed in the upper right and left, and lower left quadrants; a 12 mm trocar was placed in the right lower quadrant. Spotty endoscopic cautery was performed just around the lesion. A circumferential incision into the mucosa was made after the submucosal injection of glycerol. Subsequently, serosal markings were made by laparoscopic surgery under endoscopic guidance. Keeping the surgical sponge retained inside, the seromuscular layer was continuously sutured, allowing inversion of the lesion. Finally, the seromuscular layer was dissected by endoscopy until its complete removal. The lesion was orally extracted using an endoscopic retrieval device. The frequency of successful en bloc resection, the duration of the procedure and the incidence of complications were evaluated.
**Results:** The clinicopathological characteristics were as follows: Study subjects comprised a male and three females with a median age of 66 years (range, 56–68). The median size of the tumor was 16.5 mm (13–20). Three lesions were located in the upper third, and one in the middle third of the stomach [A1]. A preoperative diagnosis was obtained in all cases. A forceps biopsy led to a GIST diagnosis in two cases with delle, whereas endoscopic ultrasound-guided fine-needle aspiration was needed in two cases without delle. En bloc resection was achieved in all cases, with a median procedure duration of 218 min (188–280). Intraoperative perforation occurred in one case at the greater curvature in the upper third of the stomach [A2], and was successfully managed by laparoscopic suturing. No cases developed postoperative complications such as bleeding, pneumonia, anastomosis insufficiency, delayed gastric empting, or surgical site infection. All patients commenced oral intake on postoperative day 2 and were discharged after median postoperative hospital stays of 9 days (8–10).
**Conclusion:** Closed LECS could be one of the treatment options for gastric GIST, especially in patients with delle.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1587 GASTROINTESTINAL STROMAL TUMORS IN THE STOMACH - LONG-TERM PROGNOSIS AFTER CURATIVE RESECTION


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**Introduction:** Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors that arises from the gastrointestinal tract, [1]GISTs originate from interstitial cells of Cajal, intestinal pacemaker cells in the gastrointestinal tract. Gastrointestinal stromal tumors (GISTs) in the stomach are characterized by diverse spectrum of morphological and clinical features, ranging from benign to malignant.
**Aims & Methods:** The aim of this study was to evaluate the prognosis of gastric GISTs after curative resection. A total of 155 patients underwent surgery for gastric GIST at Pusan National University Hospital between February 2001 and June 2012. Of them, 10 patients were excluded because of other concomitant malignancy such as gastric cancer. Clinicopathologic features such as age, gender, tumor location, tumor size, mitotic count(/50 high power field [HPF]), histopathologic finding (spindle, epithelioid, mixed), National Institutes of Health(NIH) classification, 7th UICC/AJCC TNM system and recurrence were retrospectively analyzed.
**Results:**

| | N = 145 (%) |
|---|---|
| Median FU duration (month, range) | 43.9 (6.1–144.1) |
| Recurrences | |
| Yes | 9 (6.2) |
| No | 136 (93.8) |
| NIH classification | |
| Very low | 0/25 (0) |
| Low | 0/65 (0) |
| Intermediate | 3/23 (13.0) |
| High | 6/33 (18.2) |
| 7th UICC/AJCC TNM system | |
| I | 1/96 (1.0) |
| II | 3/34 (8.8) |
| IIIA | 4/10 (40) |
| IIIB | 1/5 (20) |
| Recurrent site (N = 11) | |
| Liver | 5 (45.5) |
| Peritoneum | 3 (27.3) |
| Spleen | 2 (18.2) |
| Operation site | 1 (9.1) |

A total of 145 patients were included into final analysis: 64 males and 81 females, with a mean age of 58.0 years. The median tumor size was 3.1 cm (range, 0.7−26 cm). Complete surgical resection was performed in 144 patients (99.3%): one case was ruptured GIST at the time of diagnosis. During median follow-up period of 43.9 months (6.1−144.1 months), 11 recurrent lesions were observed in 9 patients. The most common site was the liver (45.4%), followed by the peritoneal cavity (27.3%), operation site (18.2%) and spleen (9.1%), respectively. According to the NIH classification, all 9 cases were intermediate or high risk group: 3 of 23 intermediate risk cases (13.0%) and 6 of 33 high risk cases (18.2%). According to the 7th UICC/AJCC TNM system, 1 case of tumor

recurrence occurred in stage I, 3 cases in stage II, 4 cases in stage IIIA, 1 case in stage IIIB. The recurrence rate of each stage was 1.0% in stage I, 8.8% in stage II, 40% in stage IIIA, 20% in stage IIIB.
**Conclusion:** The recurrence occurred in the 9 patients. The recurrence rate of gastric GISTs after curative resection was 6.4%. Almost recurred cases occurred in the advanced stage, but this rate was lower than that of previous Western reports.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1588 IS RADICAL SURGERY NECESSARY IN ALL PATIENTS WHO ARE DIAGNOSED WITH EARLY GASTRIC CANCER WITH DEEP SUBMUCOSAL INVASION? RETROSPECTIVE STUDY IN A SINGLE CENTER


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**Introduction:** The indication of Endoscopic submucosal dissection (ESD) for early gastric cancer has been extended on the basis of non-inferiority to a treatment outcome of the surgical resection. Therefore, radical surgery is routinely performed for patients who do not meet the curative criteria for ESD due to the risk of lymph node metastasis (LNM). However, this standard therapeutic option may be excessive given the lower number of patients with LNM.
**Aims & Methods:** The purpose of this study is to investigate the clinicopathological factors that influence the probability of LNM in early gastric cancer with deep submucosal (SM) invasion. We reviewed 119 consecutive patients who were diagnosed with early gastric cancer with deep SM invasion after gastrectomy and lymph node dissection between November 2007 and February 2016. Of 119 cases, 19 were performed ESD before gastrectomy. In this study, according to curative criteria for ESD, we determined a deep SM invasion as a depth for more than 500$\mu$m from the muscularis propria. Statistical calculations were performed using SPSS (version 22, Chicago, IL, United States). The data were statistically analyzed using the chi-squared test and an unpaired Student's t test. The independent factors for LNM were analyzed by binary logistic regression analysis.
**Results:** The patient characteristics as follows; male/female: 89/39, mean age $68.8 \pm 11.8$, histological subtype: intestinal/diffuse/gastric carcinoma with lymphoid stroma 69/40/10, location: lower third/middle third/upper third 62/38/19. Of 119 cases, 29 (24.4%) showed LNM. Increased tumor size ($p = 0.001$), lymphovascular invasion($p < 0.001$), the poorly differentiated component ($p < 0.001$), and women ($p = 0.021$) were associated with LNM. Otherwise, gross type, depth of invasion, histological subtype, and location were not associated with LNM. Furthermore, we investigated the independent predictive risk factors for LNM using binary logistic regression analysis. Tumour size ($p = 0.001$, adjusted Odds ratio (OR): 1.05), lymphovascular invasion ($p = 0.025$, adjusted OR: 7.92), and the poorly differentiated component ($p = 0.025$, adjusted OR: 6.43) were independent predictive risk factors for LNM in early gastric cancer with deep SM invasion.
**Conclusion:** Our data represented that lymphovascular invasion and the poorly differentiated component are important factor for the risk of LNM in the gastric cancer with deep SM invasion. This means that no additional treatment after ESD may be an acceptable option for deep SM invasive gastric cancer without those two risk factors. In the near future, appropriate personalized treatment strategies must be required strongly all over the world. As a matter of course, not all patients with deep SM invasive gastric cancer may need for radical surgery.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1589 ANALYSIS OF MICROVASCULAR DENSITY IN GASTRIC TUMOR USING MAGNIFYING ENDOSCOPY COMBINED WITH A NARROW-BAND IMAGING SYSTEM


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**Introduction:** Differential diagnosis between early gastric carcinoma and low-grade adenoma (LDA) is difficult by conventional endoscopy. The narrow-band imaging (NBI) system allows endoscopic observation of minute microvessels in the gastric mucosa. However several studies have reported characteristics of microvessels in gastric carcinoma by magnifying endoscopy with NBI (ME-NBI), differentiation between gastric carcinoma and LDA observed by ME-NBI is still unknown.
**Aims & Methods:** This study aimed to evaluate the microvascular density of gastric tumors (gastric carcinoma and LDA) using ME-NBI. Forty-two differentiated type carcinoma, 10 undifferentiated type carcinoma and 5 LDA were evaluated. The microvessels observed using ME-NBI were extracted from stored still images and the microvascular density was analyzed. Histological vascular density in resected specimens was also evaluated using CD34 immunostaining.
**Results:** The color of tumor appeared mainly reddish in the carcinoma and discolored in the LDA. There were significant differences between the microvascular density in carcinoma and LDA ($8.92 \pm 4.85\%$ vs $1.96 \pm 0.96\%$; $P < 0.01$) using ME-NBI. Vascular density assessed histologically also differed significantly between carcinoma and LDA in both the whole mucosal ($5.32 \pm 3.06\%$ vs $2.24 \pm 0.67\%$; $P < 0.05$) and the superficial mucosal layers (0–100 $\mu$m) ($5.86 \pm 3.57\%$ vs $2.05 \pm 0.49\%$). There was good agreement between ME-NBI and histologically assessed microvascular density in both the whole ($r = 0.667$; $P < 0.001$) and superficial mucosal layers ($r = 0.673$; $P < 0.001$). White opaque substance (WOS) were seen in eight patients of carcinoma and 4 patients of LDA. In almost all cases with WOS, the appearance of the carcinoma was discolored.
**Conclusion:** There was a close relationship between ME-NBI assessed microvascular density and histologically assessed vascular density in mucosal layer. Microvascular density differed significantly between the gastric carcinoma and LDA assessed using ME-NBI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1590 POORLY COHESIVE CARCINOMA OF EARLY GASTRIC CANCER, IS ENDOSCOPIC TREATMENT REALLY RISKY?


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**Introduction:** Poorly cohesive carcinoma (Signet ring cell carcinoma, SRC) is a poorly differentiated cancer of the stomach. Generally, poorly differentiated cancer is believed to show poor prognosis and aggressive behavior. Recently, however, there is debate on the aggressiveness of SRC in early gastric cancer (EGC). We therefore studied post-operation biopsies to investigate the aggressiveness of SRC in EGC.
**Aims & Methods:** We reviewed medical records of patients with EGC who had surgery from January 2011 to December 2015 in a tertiary hospital in Daejeon, South Korea. We evaluated the histologic type, invasion depth, lymphatic invasion and lymph node(LN) metastasis after surgery.
**Results:** 823 EGC lesions from 789 patients were studied. 497 patients had well to moderate differentiated cancer while 65 had poorly differentiated cancer, 187 had SRC, 26 had poorly differentiated with SRC, 37 had mixed type, and 10 patients had medullary carcinoma. LN metastasis was associated with the histologic type of EGC ($p = 0.000$). 9% of differentiated cancer, 21.5% of poorly differentiated cancer, 10.2% of SRC, 11.5% of poor differentiation with SRC, 29.7% of mixed type and 20% of medullary type showed LN metastasis. The risk of SRC was not higher than well to moderated differentiated cancer ($OR = 1.1$, $p = 0.658$). Risk of mixed cancer was highest compared with differentiated cancer ($OR = 4.25$, $p = 0.000$). Risk of lympathic invasion was also similar with LN metastasis. Compared with differentiated cancer, Odds ratio of SRC was 0.79 ($p = 0.191$). There was no LN metastasis in SRC below $< 1$ cm (0/27). 5 LN metastasis were found only in SRC below $< 2$ cm (5/102, 4.9%). 3 LN metastasis were found in

mucosal cancer of SRC (3/120, 2.5%) and 2 LN metastasis in SM1 cancer (2/17, 11.76%).
**Conclusion:** Our results show that LN metastasis and lymphatic invasion is not more aggressive in SRC when compared to differentiated cancer. SRC may be considered a candidate for endoscopic treatment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1591 LYMPHOCYTIC GASTRITIS IS PRESENT IN CELIAC DISEASE AND IMPROVES AFTER GLUTEN-FREE DIET

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**Introduction:** Chronic gastritis appears to be more common in patients with celiac disease (CD).
**Aims & Methods:** Aim of this study is to evaluate the frequency of lymphocytic gastritis (LG), chronic active gastritis (CAG) and chronic inactive gastritis (CIG) in a cohort of patients with CD, and their histological changes after treatment with a gluten-free diet. Methods: A five-year prospective study including all consecutive patients with a new diagnosis of CD performed at our GI Unit, in the period between January 2010 and January 2015. All gastric and duodenal biopsy specimens at the time of the diagnosis of CD and at the first endoscopic control after 18–24 months on gluten-free diet were analyzed. CD diagnosis was made in the presence of anti-tissue transglutaminases and/or anti-endomisial antibodies associated with specific alterations at histological evaluation of duodenal biopsies, according to the modified Marsh-Oberhuber classification. Gastric lesions were classified according to the Updated Sydney System. Giemsa staining was used for histological diagnosis of *Helicobacter pylori* infection and immunohistochemical staining for the diagnosis of LG, defined as a dense proliferation of intraepithelial lymphocytes (more than 25 lymphocytes per 100 epithelial cells). Anti-gastric parietal cell antibodies were assayed by enzyme-linked immunosorbent assay (ELISA). Demographic, clinical, and laboratory data were collected.
**Results:** 250 patients with CD were enrolled (191 F, 59 M, mean age 34 years at the diagnosis). At the time of CD diagnosis, histological examination showed normal gastric mucosa in 78 patients (31.2%), LG in 32 (12.8%), CAG in 74 (29.6%), and CIG in 66 (26.4%). Out of 32 patients with LG, 20 (62.5%) were *H. pylori* negative and all of them showed an improvement of gastritis after gluten free diet. Out of 74 patients with CAG, 30 (40.5%) were *H. pylori* negative and one third of them showed an improvement of gastritis after gluten-free diet. Out of 66 patients with CIG, 63 (95.4%) patients were *H. pylori* negative. LG is significantly associated to histological improvement after gluten-free diet compared to other types of gastritis ($p = 0.0039$).
**Conclusion:** Subtypes of gastritis have different probability to be influenced by the gluten-free diet. LG is present in a significant number (13%) of CD patients and seems to improve as well as duodenal lesions after gluten-free diet. Two-thirds of LG are not associated with *H. pylori* infection. Both CAG and CIG are also significantly associated with coeliac disease, despite less influenced by gluten-free diet.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1592 THE INCIDENCE OF SELF-MEDICATION OF UPPER-GASTROINTESTINAL SYMPTOMS IN ALBANIAN COMMUNITY PHARMACIES

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**Introduction:** Upper-gastrointestinal (GI) symptoms are a common reason for self-treatment with Over the Counter medications. (OTC). However data are scarce on the typology of GI complaints for which individuals seek self-medication and more importantly, on the prevalence of the alarm symptoms in this population.
**Aims & Methods:** The aim of this study was to investigate the: a. the nature of GI symptoms that people intend to self-medicate b. the prevalence of alarm symptoms c. adherence to referral advice given by the pharmacist d. self-reported efficaccy and frequency of use of OTC medication for minor complaints. Methods: This descriptive study was conducted in 13 pharmacies located in Tirana, the capital of Albania. the study was conducted from November 2015 till January 2016. Participants ($N = 192$) completed a questionnaire to assess symptoms characteristics and previous medical consulting. Based on this information the pharmacist referred subjects to the physician or advised for self-treatment. Four weeks later, participants were presented a follow-up questionnaire evaluating their adherence to referral advice or efficaccy of self-treatment.
**Results:** The most frequently reported GI symptoms were burning retrosternal discomfort (39.2%), acid regurtation (56.2%) and postprandial fullness (61.2%). At least one alarm symptom was present in 22.4% of the individuals, with difficulty in swallowing being the most prevalent (14.4%). Although 21% of the patients were referred, only 41.7% of them contacted a physician. Almost all (95.1%) of the remaining customers who were advised self-treatment reported symptom relief with the OTC drug obtained.
**Conclusion:** Mild gastrointestinal symptoms will mostly resolve with self-treatment. Yet, the value of pharmacist counseling on OTC treatment should be recognized, as community pharmacist can play an important role in distinguishing symptoms that warrant further medical examination.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1593 SHOULD GENERAL PHYSICIANS/INTERNISTS OR GI SPECIALISTS MANAGE PEPTIC ULCER DISEASE?

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**Introduction:** *H. pylori* is the cause of >90% of duodenal ulcers (DU) and >60% gastric ulcers (GU) with eradication of infection curing the ulcer diathesis and preventing recurrence. National UK guidelines recommend testing for *H. pylori* in all patients with DU & GU and treating those found to be infected[1].
**Aims & Methods:** To assess if patients with PUD are being cured by eradication of *H. pylori*. Methods: analysis of endoscopy database with linked electronic case note review from 2012–2106. *H. pylori* status was assessed by CLO-test or using stool antigen (HpSA) prior to treatment. Eradication was assessed by $^{13}$C-Urea Breath test or repeat HpSA at least 6 weeks after finishing treatment.
**Results:** From Dec 2012-March 2016, 413 patients (69% men, mean age 59yr range 12–95yrs), were found to have DU ($n = 209$), GU ($n = 186$) or both ($n = 18$) at the time of their endoscopy. 52% of patients were inpatients, of whom 33% were undergoing OGD due to upper GI bleeding. Overall CLO test was done in 263/413 (76%) with results available for 53% of whom 37% were positive. However only 62% of those found to be infected were given eradication therapy. Subsequently a UBT test to assess eradication occurred in only 50% (HpSA in 3%), and was negative in only 76%. Analysis of the data by supervising speciality showed the following:

Outcomes by general internist vs GI specialist

| | Generalist / Internist | GI specialist | Significance ($\chi^2$) |
|---|---|---|---|
| DU(n)/GU(n)/PU(n) | 169/164/12 | 40/22/6 | |
| CLO-test taken | 263/345 (76%) | 68/68 (100%) | $p < 0.0001$ |
| CLO-test result available | 147/345 (43%) | 68/68 (100%) | $p < 0.0001$ |
| CLO-test positive | 96/147 (65%) | 68/68 (100%) | $p = 0.01$ |
| Hp eradication given | 96/96 (100%) | 68/68 (100%) | |
| patients lost to follow-up | 60/96 (63%) | 8/68 (12%) | $p < 0.0001$ |
| Hp eradication assessed | 36 | 60 | |
| % eradicated | 17/36 (47%) | 56/60 (94%) | $p < 0.0001$ |
| NICE standard achieved | 17/96 (18%) | 56/68 (82%) | $p < 0.0001$ |

**Conclusion:** The opportunity to cure peptic ulcer disease by Hp testing and eradication of *H. pylori* in those found to be infected is not being taken in patients admitted to hospital, particularly if under the care of general physicians. Patients with *H. pylori*-associated PUD should be looked after by GI specialists with an interest in *H. pylori*.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1594 IMPROVEMENT OF APPROPRIATENESS OF UPPER GI ENDOSCOPY FOR OUT-PATIENTS THROUGH SELECTION AND INTRODUCTION OF GASTROPANEL: A SINGLE-CENTRE PROSPECTIVE STUDY

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**Introduction:** Increasing the appropriateness of use of upper GI endoscopy is important to improve the quality of care while containing costs.
**Aims & Methods:** Aim of this study was to evaluate the appropriateness of upper GI endoscopy in out-patients through a strict selection of endoscopy prescriptions, Gastropanel introduction and endoscopic activity reorganization. A total of 5192 upper GI endoscopy requests were prospectively evaluated from July 2013 to July 2015. The upper GI endoscopy reservation was managed by our Endoscopy Unit and all the prescriptions were evaluated by a senior endoscopist. All the requests were evaluated within 24 hours. The endoscopist evaluated if the prescription was appropriated and decided the timing. In some cases, the endoscopist could either cancel the request or chose a less invasive examination (i.e. Gastropanel) which evaluates serum levels of gastrin 17 (G17), Pepsinogen I (PGI) and II (PGII) and *Helicobacter pylori* (Hp) antibodies.
**Results:** 540 of 5192 upper GI endoscopy requests (10.4%, age 50 years, range 14–91) were judged inappropriate. The cancelled requests were due in 66 cases for dyspepsia, 307 for gastroesophageal reflux disease (GERD), 34 for cases without written indication, 113 for wrong follow-up, 20 for other indications. 282 of 540 patients did Gastropanel and showed in 94 normal values, in 48 normal values but in PPI therapy, in 56 an Hp infection, in 30 an Hp eradication, in 50 GERD and in 4 an atrophic gastritis. In the last 4 cases, an upper GI endoscopy was done immediately after Gastropanel reporting. 105 of 540 cancelled requests performed a upper GI endoscopy within 2 years (range 1–22 months) after evaluation: 71 of 105 (67.5%) were normal and no cancer was found.
**Conclusion:** This strategy, based on a strict control of the prescription, is effective to increase the appropriateness without any additional public cost. The use of Gastropanel improves patient selection for upper GI endoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**H. PYLORI III – POSTER EXHIBITION**

### P1595 CLINICAL, HISTOPATHOLOGICAL, IMMUNOLOGICAL AND MICROBIOLOGICAL CHARACTERIZATION IN A COHORT OF PATIENTS OF TREATMENT-RESISTANT HELICOBACTER PYLORI INFECTION

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**Introduction:** Eradication of *Helicobacter pylori* (HP) with acid inhibitors and antibiotics have a success rate of 90%. Unfortunately, resistance to the treatment has been seen despite treatment with various antibiotic regimes [1].
**Aims & Methods:** Aims • To describe the clinical, pathological, microbiological and immunological phenotypes in patients resistant to repeated and various treatment regimes. • To examine the effect of levofloxacin on the efficacy to obtain eradication of HP. Methods There were 4 groups of patients: Group 1: HP treatment resistant after at least two different treatment regimes where patients were included: Group 2: patients with newly diagnosed HP infection; Group 3: patients with previously treated to eradication of HP infection Group 4: patients with normal endoscopy including HP status. Group 1 and group 2 were both treated with acid suppressive agent whereas the antibiotic regime was amoxicillin/levofloxacine and amoxicillin/clarytromycin, respectively. The gastric biopsies were analysed for histological changes according to the Sidney classification, mucosal gene-expressions of TH1, TH2, TH17 og T-reg cytokines performed byRT-PCR technique, whereas HP resistance were examined according to conventional methods.
**Results:** The number of patients included were 42, 50, 61and 32 in the four groups, respectively. No significant differences were found in dyspeptic symptoms between the groups. HP was successfully eradicated in 89% and 73% in group 1 and Group 2, respectively. Sydney classification showed significant higher infiltration of neutrofils and monocytes in group 2 compared to group 1, 3 and 4. When comparing the cytokines, the resistant group had significantly lower gene transcript for TNF alpha and IL.10, whereas significantly higher gene transcript for all cytokines were observed when compared to the previously eradicated group and no infection group (table 1). In group 1 there was more clarithromycin and metronidazole resistance than in group 2 at non-significant level, tetracyclin resistance was low in both groups whereas Amoxicillin resistance was not observed in any of the Groups. In the control endoscopy after treatment metronidazole resistance was observe in 1 patient in group 1, and clarythromycin and metronidazole resistance were observed in 1 and 3 patients, respectively.

**Table 1:** Gene expression in groups relative to the resistant infection Group

| Gene | ANOVA P | Newly diagnosed | Previously eradicated | No infection |
|---|---|---|---|---|
| **TNF alpha** | <0.0005 | 2.2(1.4–3.4)* | 0.36(0.22–0.58)* | 0.54(0.34–0.87)* |
| **IL17A** | <0.0005 | 1.9(0.9–3.9)n.s. | 0.13(0.06–0.30)* | 0.07(0.03–0.25)* |
| **IL33** | 0.001 | 1.2(0.8–1.9)n.s. | 1.8(1.1–3.0)* | 2.8(1.7–4.5)* |
| **IL10** | <0.0005 | 3.0(1.7–5.2)* | 0.31(0.16–0.60)* | 0.33(0.18–0.61)* |
| **TGFB1** | <0.0005 | 1.3(0.9–1.8)n.s. | 0.53(0.37–0.76)* | 0.64(0.45–0.91)* |
| **TBX** | <0.0005 | 1.3(0.9–1.9)n.s. | 0.43(0.28–0.65)* | 0.62(0.41–0.95)* |
| **FOXP3** | <0.0005 | 2.4(1.4–4.1)* | 0.34(0.18–0.62)* | 0.38(0.21–0.67)* |

Values are fold difference (95% CI) P value for contrast vs. the resistant infection group. Asterisk indicates significant contrast.
**Conclusion:** Levofloxacine is highly effective to eradicate HP in previously treatment- resistant patients. This treatment- resistant cohort had a lower histological inflammation, lower proinflammatory cytokine profile, and high resistance against clarithromycin and metronidazole compared to the cohort of newly diagnosed HP.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1596 H. PYLORI-SPECIFIC INDUCTION OF TH17 IMMUNE RESPONSE

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**Introduction:** *H. pylori* infection leads to chronic gastritis with further development of premalignant conditions (atrophy, intestinal metaplasia), which are the known risk factors for gastric cancer. Besides bacterial virulence factors the inflammatory mucosal micromilieu determines the course of gastritis. The mucosal Th17 response has been suggested to crucially influence malignant progression but has not been studied in detail in humans.
**Aims & Methods:** To characterize the human mucosal Th17 response ex vivo and *H. pylori*-specific activation of human CD4+ T cells in vitro. Analysis of mucosal gene expression and immunohistochemical staining of RORyt and IL-17 in antrum mucosa of 66 *H. pylori*-negative and 91 *H. pylori*-positive prospectively recruited patients. We established a human in vitro system using *H. pylori*-specific (*H. pylori* BCM300) antigen presenting cells (APC) to activate CD4+ T cells. APC and CD4+ T cells were isolated from human PBMC of *H. pylori*-negative donors. Th17 immune response was analyzed by IL-17 protein secretion and gene expression in CD4+ T cells as well as STAT3/p-STAT3 pathway in CD4+ T cells upon activation with *H. pylori*-specific APCs by WB analysis.
**Results:** *H. pylori*-positive patients showed 2.8–14.4-fold gene expression of RORyt and IL-17 in antrum mucosa. These findings were confirmed by immunohistochemistry demonstrating infiltrating CD4/RORyt positive T cells in the mucosa of *H. pylori*-infected patients. In in vitro model, *H. pylori*-specific activation of CD4+ T cells leads to induction of IL-17 gene expression and IL-17 secretion. Furthermore, we demonstrate the *H. pylori*-dependent activation of STAT3/p-STAT3 pathway that is crucial for Th17 development and immune response.
**Conclusion:** The inflammatory micromilieu determine the course of *H. pylori* gastritis. For malignant progression Th17 immune response is discussed as a promoting condition in animal models. This is one of the first studies characterizing mucosal *H. pylori*-specific Th17 immune response in human CD4+ T cells using ex vivo and in vitro models.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1597 CURCUMIN UPREGULATES INDOLEAMINE 2,3-DIOXYGENASE (IDO) AND DOWNREGULATES INTERLEUKIN (IL)-17 PRODUCTION IN HELICOBACTER PYLORI-INFECTED HUMAN GASTRIC MUCOSA

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**Introduction:** IL-17 plays a role in the host response against *H. pylori* and, possibly, in its clearance/persistence. We demonstrated that an enhanced expression of IDO, the enzyme promoting the effector T-cells apoptosis and the differentiation of regulatory T cells, downregulates Th17 pathway in *H. pylori*-infected human gastric mucosa. The phytochemical compound curcumin was suggested as an anti-*H. pylori* agent due to its anti-inflammatory, anti-oxidant and anti-microbial properties.

**Aims & Methods:** Five antral biopsies were taken from 11 patients (6 M, median age 51 years, range 20–74) who underwent upper gastrointestinal endoscopy for dyspeptic symptoms: 1 for urease quick test (Eurospital, Trieste, Italy), 2 for histology (Giemsa staining for *H. pylori* and modified Sydney System for gastritis score), and 2 for organ culture. A C13-urea breath test was also performed (at least two tests positive and all the three tests negative to be considered *H. pylori*-infected or uninfected). Biopsy samples were immediately placed in an organ culture chamber and treated with and without curcumin 200 μM (Sigma, St. Louis, MO, USA) for 6 hours and 20 hours. Preliminary experiments were performed in order to optimize the time course (4, 6, 12, 20 and 24 hours). The expression of IDO protein and that of IL-17 were determined by Western blotting in total proteins extracted from gastric biopsy cultures, after 6 and 20 hours, respectively. The ratio of IDO and IL-17 with beta-actin was calculated by densitometry and values expressed as means ± SD arbitrary units (a.u.).

**Results:** As expected, inflammatory changes were more severe in gastric mucosal samples from *H. pylori*-infected ($n = 7$) than uninfected ($n = 4$) patients (gastritis score $5.8 \pm 1.9$ vs $1.4 \pm 1.5$, $p < 0.01$). IDO significantly increased in *H. pylori*-infected gastric mucosal samples treated with curcumin compared with untreated samples ($0.71 \pm 0.20$ a.u. vs $0.38 \pm 0.11$ a.u., $p = 0.01$). In the same patients, a significant reduction in IL-17 levels was found in samples treated with curcumin compared with those untreated ($0.37 \pm 0.18$ a.u. vs $0.53 \pm 0.20$ a.u., $p = 0.004$). Levels of both IDO and IL-17 were very low in untreated *H. pylori*-uninfected samples and did not significantly change in curcumin-treated samples.

**Conclusion:** This study demonstrates, for the first time, that curcumin enhances IDO expression and downregulates IL-17 production in *H. pylori*-infected human gastric mucosa. This could be part of the complex anti-inflammatory effect exerted by curcumin, supporting the potential immunomodulatory role of the compound in *H. pylori* infection.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1598 DECREASED GHRELIN RELEASE: POTENTIAL LINK BETWEEN HELICOBACTER PYLORI INFECTION AND CARDIOVASCULAR DISEASE?

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**Introduction:** Both HP infection and decreased ghrelin release have been shown to increase the risk of cardiovascular (CV) disease. Thus, it is intriguing to speculate that HP-induced atrophic gastritis with reduced release of ghrelin from the gastric mucosa (1) may promote CV disease in HP infection. On the other hand, ghrelin release is also associated with classical CV risk factors such as obesity and diabetes.

**Aims & Methods:** We aimed to clarify whether HP infection is an independent risk factor for decreased interdigestive and postprandial ghrelin release. Patients received a 420 kcal test meal. Blood samples for ghrelin and blood glucose measurements were drawn at regular intervals for 3 hours. Traditional CV risk factors including age, gender, body mass index (BMI), total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides, HbA1c, smoking habits, family history, prevalence of arterial hypertension and diabetes were evaluated. Carotid intima-media thickness was determined sonographically. HP infection was diagnosed based on specific immunological and/or histological testing.

**Results:** 58 subjects were included (39 females). Fasting and postprandial ghrelin release correlated inversely with fasting and postprandial blood glucose concentration as well as with HbA1c ($p < 0.05$). Accordingly, diabetics ($N = 13$) had significantly lower ghrelin release than patients without diabetes. Furthermore, postprandial ghrelin release was inversely correlated with BMI ($p = 0.005$) and LDL ($p = 0.02$) and was directly associated with HDL ($p = 0.0004$). Males ($N = 19$) had significantly lower postprandial ghrelin release than females ($N = 39$) (mean ± SEM: $462 \pm 37$ vs. $659 \pm 42$ pg/mL, $p = 0.001$) and ghrelin was significantly reduced in HP-positive patients ($N = 16$) ($468 \pm 36$ vs. $661 \pm 41$ pg/mL, $p = 0.001$). Multivariate linear regression analysis revealed that only sex and HP status were independent predictors of postprandial ghrelin release.

**Conclusion:** Decreased ghrelin release in HP infection is not a consequence of its association with classical CV risk factors such as disturbed blood glucose control, dyslipidemia and obesity. Since ghrelin exerts protective effects on the CV system, its impaired release may be of pathophysiological importance for explaining the association between HP infection and CV disease.

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## P1599 THE PREDICTORS OF THE GASTRODUODENAL ZONE EROSIVE-ULCERATIVE LESIONS DEVELOPMENT IN PATIENTS WITH LEUKEMIA

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**Introduction:** Patients with acute (AL) and chronic leukemia (CL) during chemotherapy have high risk of the secondary polyorganic complications development. The development of erosive-ulceretive lesions (EUL) of mucosal layer in gastroduodenal zone (GDZ) limits the dose maintenance and cytotostatic therapy regimes, aggravate early and late chemotherapy results.

**Aims & Methods:** We aimed to examine the role of impaired resistance mucosal barrier in the GDZ EUL development in patients with AL and CL. Material and methods: 159 patients with AL and CL were examined and divided into 2 groups depending on types of leukemia: I ($n = 78$) – AL patients; II ($n = 81$) – CL patients, aged 17–77 years; 87(54.7%) males, 72(45.3%) females. During the 1st course of chemotherapy the presence of chronic gastritis (CG), ulcer disease (UD), *Helicobacter pylori* (HP) infection, mucosal barrier status was assessed. The patients groups I and II were divided into subgroups according to the upper endoscopy Results: I-A ($n = 44$) – AL patients without GDZ EUL; I-B ($n = 34$) – AL patients with GDZ EUL; II-A ($n = 62$) – CL patients without GDZ EUL; II-B ($n = 19$) – CL patients with GDZ EUL. Mucosal barrier status was estimated by the concentations of N-acetylneuraminic acid (NANA) in serum and the level of its excretion in the urine, protein-bound and unbound fucose concentration in blood serum and fucose urinary level before chemotherapy.

**Results:** By the clinical records the presence of the chronic GI diseases in 24 (30.7%) AL patients I and 35 (43.2%) CL patients II groups was estimated, HP-infection – in 47 (60.2%) AL patients of group I and 54 (66.6%) CL patients of group II. EUL on upper GI segment were revealed in 34 (43.6%) patients of I and in 19 (23.4%) patients of II groups, in 16 (47%) and 15 (78.9%) patients of them were estimated CG, UD, HP-infection – in 28 (82.3%) and 17 (89.4%) respectively. During assessment of mucosal barrier status the increased serum NANA concentration in 1.2 times was noticed in patients of I-A subgroup, in I-B and II-B subgroups with EUL in GDZ during chemotherapy – in 1.3 times ($p < 0.05$) compared with normal. The level of NANA excretion was elevated in patients of I-A, II-A subgroups in 1.36 and 1.34 times and in patients of I-B, II-B subgroups in 1.5 and 1.4 times compare with normal ($p < 0.01$). In patients of I-A, II-A subgroups protein-bound fucose concentration decreased in 1.5 and 1.36 times respectively ($p < 0.05$), and in patients of I-B, II-B subgroups in 2,5 and 2 times respectively ($p < 0.01$) compared with normal values. The level of fucose urinary excretion in pts of I-A, II-A subgroups decreased in 1.2 and in patients of II-A, II-B subgroups – in 2 and 1,9 times respectively ($p < 0.001$) compared with normal.

**Conclusion:** In patients with acute and chronic leukemia the highest risk of the GDZ EUL development was observed in patients with CG, UD, HP-infection in anamnesis, that was accompanied with impaired resistance of GDZ mucosal barrier. The impairment barrier function is characterized by increased sialoproteins degradation, decreased fucoproteins synthesis. It can be considered as the risk factor of the GDZ EUL of mucosal layer development during chemotherapy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1600 COMPARISON BETWEEN A POTASSIUM-COMPETITIVE ACID BLOCKER AND A PROTON PUMP INHIBITOR FOR THE EFFICACY OF HELICOBACTER PYLORI ERADICATION IN JAPANESE PATIENTS

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**Introduction:** *Helicobacter pylori* (*H. pylori*) is one of the most prevalent bacterial pathogens and is associated with upper gastrointestinal disorders such as gastritis, peptic ulcers, functional dyspepsia, gastric mucosa-associated lymphoid tissue lymphoma, and gastric cancer [1][2][3]. Eradication of *H. pylori* infection is reported to provide an effective approach to curing or preventing these *H. pylori*-associated diseases [4][5]. In Japan, 7-day triple therapy for *H.*

*pylori* including clarithromycin (CAM) was approved in 2000. However, antibiotic resistance subsequently reduced this rate to an unacceptable level (70%). Vonoprazan, an orally bioavailable potassium-competitive acid blocker (P-CAB), was approved in 2014 for use in Japan. This could improve eradication rates by increasing the intragastric pH, thus increasing bacterial antibiotic susceptibility.

**Aims & Methods:** This study compared the efficacy of 7-day triple therapies that included amoxicillin, CAM, and P-CAB or proton pump inhibitor (PPI). We prospectively analyzed *H. pylori* eradication rates in 146 patients receiving 7-day triple therapy containing P-CAB (April 2014 to September 2015), and in 1305 patients retrospectively who received 7-day triple therapy containing PPI (April 2011 to September 2015).

**Results:** *H. pylori* was eradicated in 89.7% (131/146) of P-CAB-treated patients; this was significantly higher than the PPI-treated patients (73.9%; 965/1305; $p < 0.05$). The eradication rates in P-CAB-treated CAM-sensitive and CAM-resistant patients were 100% (44/44) and 87.5% (28/32), respectively; these were significantly higher than the corresponding rates in PPI-treated patients (88.0% [22/25] and 53.8% [7/13], $p < 0.05$).

**Conclusion:** P-CAB improved the efficacy of CAM-containing 7-day triple therapy in patients with CAM-resistant *H. pylori*. P-CAB is considered to exceedingly develop the strategy for *H. pylori* eradication worldwide.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1601 EFFICACY AND TOLERABILITY OF A TRIPLE THERAPY CONTAINING A POTASSIUM-COMPETITIVE ACID BLOCKER AS FIRST-LINE TREATMENT FOR HELICOBACTER PYLORI INFECTION


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**Introduction:** Potassium-competitive acid blocker (P-CAB) is a new class of gastric acid inhibitory agents. Vonoprazan (VPZ) is a novel, orally active P-CAB. The acid inhibitory effect of VPZ was shown to be greater than that of proton pump inhibitor (PPI). However, the efficacy of VPZ for *Helicobacter pylori* (*H. pylori*) eradication treatment remains unknown.

**Aims & Methods:** This study evaluated the efficacy and tolerability of VPZ as first-line *H. pylori* eradication treatment compared with PPI-based triple therapies. We retrospectively reviewed the medical records of 733 consecutive patients who received first-line *H. pylori* eradication treatment at Yuri Kumiai General Hospital between January 2013 and January 2016. Patients who received 7-day VPZ-based therapy (vonoprazan 20 mg + amoxicillin 750 mg + clarithromycin 200 mg twice/day) were compared with those who received 7-day lansoprazole (LPZ) or rabeprazole (RPZ) based therapies (lansoprazole 30 mg / rabeprazole 20 mg + amoxicillin 750 mg + clarithromycin 200 mg twice/day). The successful eradication and adverse event rates of VPZ therapy were compared with those of LPZ or RPZ therapies.

**Results:** Among 733 patients who received first-line *H. pylori* eradication treatment, 253 patients were received VPZ therapy, 402 patients were received LPZ therapy, and 78 patients were received RPZ therapy. The eradication rates of VPZ therapy were significantly higher than both LPZ and RPZ therapies in intention-to-treat (87.8% vs. 74.1%; $p < 0.001$ / 87.8% vs. 74.4%; $p = 0.004$,) and per-protocol analyses (90.2% vs. 78.0%; $p < 0.001$ / 90.2% vs. 77.3%; $p = 0.003$). There was no significant difference in the incidence of adverse events between the three therapies except skin rash. The incidence of skin rash was significantly higher with VPZ than with LPZ therapy (5.1% vs 1.5%; $p = 0.007$). No patients discontinued *H. pylori* eradication treatment because of adverse events.

**Conclusion:** 7-day VPZ-based triple therapy was more effective than 7-day PPI-based triple therapies as a first-line *H. pylori* eradication treatment. Although the incidence of skin rash was higher with VPZ therapy, 7-day VPZ-based triple therapy was generally well tolerated.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1602 A COMPARATIVE STUDY OF POTASSIUM-COMPETITIVE ACID BLOCKER (VONOPRAZAN) AND PROTON POMP INHIBITORS IN HELICOBACTER PYLORI ERADICATION THERAPY


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**Introduction:** Triple therapy, proton pomp inhibitor (PPI) combined with antibiotics for *H. pylori* eradication has been shown to be effective for *H. pylori* related upper gastrointestinal diseases. Recently, the eradication rate of the first-line treatment has been reported to decrease due to the increased prevalence of Clarithromycin (CAM) resistant, thus more effective strategy is required. Potassium-competitive acid blockers (P-CABs) are new class of gastric acid suppressant agents, which lead to more intensive and longer acid suppression than PPIs. As maintaining intragastric pH higher is crucial in *H. pylori* eradication therapy, we assume P-CABs might be more effective than PPIs in *H. pylori* eradication.

**Aims & Methods:** We retrospectively evaluated the clinical effectiveness and safety of Vonoprazan 20 mg (P-CAB)-based eradication therapy compared to conventional PPI-based therapies. We investigated data of our *H. pylori*-positive patients administered the first-line (with Clarithromycin and Amoxicillin) ($n = 1353$) and the second-line (with Metronitazole and Amoxicillin) ($n = 261$) eradication therapy from April 2014 to December 2015 at Hattori clinic. The primary endpoint was the assessment of eradication rates by Full analysis set (FAS). The secondary endpoints were the evaluations of adverse events (AE) and related factors for *H. pylori* eradication therapy.

**Results:** In the first-line treatment, the eradication rates of Vonoprazan (VPZ), Esomeprazol (EPZ), Raveprazole (RPZ) and Lansoprazole (LPZ) were 87.9% (95% CI: 84.9–90.5%), 71.6% (95% CI: 67.5–75.5%), 62.9% (95% CI: 52.0–72.9%), 57.3% (95% CI: 50.4–64.1%), respectively. The eradication rate VPZ was significantly higher than that of other PPIs ($P < 0.05$). Interestingly, smoking decreased the eradication rate (non-smoker: 68.1%, smoker; 56.6%) in PPI group ($P = 0.013$). By contrast, smoking did not affect the eradication rate (non-smoker; 87.3%, smoker; 91.3%) in VPZ group ($P = 0.34$). Sex, age, obesity, alcohol habit and the degree of atrophic gastritis were not predicting factors. The AE incidence of VPZ (61/546; 11.2%) was higher than that of EPZ (39/507; 7.7%), though there was no significant difference ($P = 0.054$). Meanwhile, there were no significant differences in the second-line treatment, including the eradication rate, predicting factors and AE incidence.

**Conclusion:** VPZ might be superior to conventional PPIs in the first-line *H. pylori* eradication therapy, especially for the smoking patients. However, it is necessary to be careful with AEs.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1603 EFFECT OF VONOPRAZAN IN TRIPLE THERAPY FOR ERADICATION OF HELICOBACTER PYLORI: INTERIM ANALYSIS OF A SINGLE-CENTRE RANDOMISED CONTROLLED TRIAL


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**Introduction:** Vonoprazan (VPZ) is new potassium-competitive acid blocker. Recently, a phase III randomised study of VPZ for eradication therapy of *Helicobacter pylori* (*H. pylori*) infection was published. The study was a non-inferiority trial that compared VPZ to lansoprazole in *H. pylori* eradication therapy. However, a comparative trial to determine the advantage of VPZ over existing acid blocker has not been conducted. We therefore performed a randomised controlled trial to confirm the effectiveness of VPZ in the eradication of *H. pylori* infection and to elucidate its advantages.

**Aims & Methods:** We aimed to determine the effectiveness and advantage of VPZ in triple therapy eradication of *H. pylori* infection. Subjects comprised patients undergoing eradication therapy for *H. pylori* infection in our hospital. Patients with a history of eradication therapy, gastrectomy, or allergy to medications in triple therapy were excluded. Written informed consent was obtained for each patient. This trial was performed as a randomised open-labelled clinical study with the permission of an institutional review board. Each patient was randomly enrolled for VPZ therapy group (VPZ 20 mg, amoxicillin 750 mg, clarithromycin 200 mg, twice a day for 7 days) or esomeprazole (EPZ) therapy group (EPZ 20 mg, amoxicillin 750 mg, clarithromycin 200 mg, twice a day for 7 days). Before starting therapy, we checked the background characteristics of each patient (age; gender; weight; height; drinking habit; smoking habit; use of probiotics, bismuth, PPI, or P-cab; and endoscopic findings). After the therapy, we asked about medication compliance and side effects. The primary endpoint was the eradication rate. The secondary endpoints were the rates of side effects. The target number of cases was 240 (120 cases in each group). Because of the ethical point of view, we performed an interim analysis when the number of cases per protocol reached 100.

**Results:** Of the 110 patients who were recruited, 10 dropped out. We allocated 57 patients to VPZ therapy group. For VPZ therapy group and EPZ therapy group, the eradication rates were 93.0% (95% confidence interval, 85.1%-100.9%) and 83.7% (95% confidence interval, 73.9%-95.5%) respectively, and the rates of side effects were 16.4% (95% confidence interval, 6.0%-26.8%) and 28.9%

(95% confidence interval, 17.2%-40.6%) respectively. For each group, no statistically significant difference in eradication rate was seen. **Discussion:** We performed an interim analysis as the number of cases per protocol reached 100. The results of univariate analysis (chi-square test) of eradication rate and rate of side effects for each therapy were p = 0.143 and p = 0.117 respectively. Although there were no statistically significant differences, the VPZ group revealed trends of high eradication rates and low rates of side effects. However, this analysis did not show any evident advantages of VPZ over EPZ; therefore, we decided to go on the current study.
**Conclusion:** The findings suggest that VPZ is effective in eradication of *H. pylori* infection. The advantage of VPZ has not yet been determined.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1604 A COMPARISON BETWEEN HYBRID AND CONCOMITANT REGIMENS FOR HELICOBACTER PYLORI ERADICATION: A RANDOMIZED CLINICAL TRIAL

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**Introduction:** *Helicobacter pylori* infection is an important issue in global health, since almost half of the world's population is infected by the organism. Also, the infection is associated with peptic ulcer disease, gastric adenocarcinoma and lymphoma.
**Aims & Methods:** Two hundred and fifty-two patients with naïve *H. pylori* infection and peptic ulcer disease were randomly divided to receive either hybrid regimen (Pantoprazole 40 mg BID and Amoxicillin 1 gr BID for 14 days, accompanied by Clarithromycin 500 mg BID and Metronidazole 500 mg BID just during the last 7 days) or concomitant regimen (Pantoprazole 40 mg, Amoxicillin 1 gr, Clarithromycin 500 mg and Metronidazole 500 mg, all twice daily for 10 days). Eight weeks after therapy, $^{14}$C- Urease Breath test was performed to confirm eradication.
**Results:** According to intention to treat analysis, the eradication rates were 87.3% (95% confidence interval = 81.4 – 93.1) and 80.9% (95% CI = 74–87.8) in hybrid and concomitant groups, respectively (p = 0.38). Per-protocol eradication rates were 89.3% (95% CI = 83.8–94.7) and 83.1% (95% CI = 76.3–89.8), respectively (p = 0.19). The rates of severe side effects were not statistically different between the two groups (4% vs. 8.7%).
**Conclusion:** Fourteen-day hybrid therapy can be considered as a nearly acceptable regimen with few severe side effects in Iran. However, it seems that the efficacy of this therapy is decreasing as the resistance rates to antibiotics are increasing. We suggest further studies to assess the efficacy of a more prolonged concomitant therapy for *H. pylori* eradication in Iran.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1605 COMPARISON OF LEVOFLOXACIN -AND CLARTHROMYCIN-CONTAINING SEQUENTIAL THERAPIES FOR HELICOBACTER PYLORI ERADICATION IN IRAN; A RANDOMIZED CLINICAL TRIAL

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**Introduction:** The prevalence of clarithromycin resistance has increased in different regions of the world and is known to be responsible for most of *Helicobacter pylori* (*H. pylori*) treatment failures. Levofloxacin-containing regimens can be used as first-line therapy in the regions that clarithromycin resistance rate is more than 20% and levofloxacin resistance rate is less than 10%.
**Aims & Methods:** We aimed the study to compare these two sequential therapies for *H. pylori* eradication in Iran. Method:One hundred and eighty-six patients with peptic ulcer disease and naive for *H. pylori* treatment, were randomized in the study. Group A; 92 patients received: esomeprazole 40 mg/bid, amoxicillin 1 gr/bid for the first 5 days, followed by esomeprazole 40 mg/bid, levofloxacin 500 mg/bid and tinidazole 500 mg/bid for the second 5 days. Group B, 94 patients received: the same regimen except for levofloxacin replaced by clarithromycin 500 mg/bid. $C^{14}$ urea breath test was done 8 weeks after the treatment for evaluation of *H. pylori* eradication.
**Results:** One hundred and seventy-two patients(86 patients in each group)completed the study. The intention-to- treat eradication rates were 85.1% (95% CI = 77.9 to 92.3) and 83.7% (95% CI = 76.2 to 91.2) (p = 0.302) and per-protocol eradication rates were 93.0% (95% CI = 87.6 to 98.4) and 90.0% (95% CI = 83.6 to 96.3) (p = 0.420) for group A and B, respectively. The compliance rate was excellent for both groups. No significant differences in incidence of adverse effects were seen between groups. One drug interruption was recorded due to severe bitter taste and nausea in group B.
**Conclusion:** Levofloxacin-containing sequential regimen showed to be safe and effective and it can be replaced by conventional sequential therapy in high clarithromycin resistance area, as a first line therapy. However, based on our recent study clarithromycin sequential therapy has had still a good eradication rate in Tehran.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1606 EFFICACY OF FIRST-LINE BISMUTH-CONTAINING QUADRUPLE THERAPIES WITH LEVOFLOXACIN OR CLARITHROMYCIN FOR THE ERADICATION OF HELICOBACTER PYLORI INFECTION: A ONE-WEEK, OPEN-LABEL, RANDOMIZED TRIAL

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**Introduction:** The aim of the present open-label, randomized control trial was to determine the clinical efficacy and safety of two one-week bismuth-containing quadruple regimens and one levofloxacin-based triple regimen for the eradication of *H. pylori* infection in treatment- naïve patients. The influence of susceptibility and host CYP2C19 polymorphisms on the efficacy was also evaluated.
**Aims & Methods:** Eligible patients were randomly to receive esomeprazole and colloidal bismuth pectin along with clarithromycin and amoxicillin (EBCA), esomeprazole and colloidal bismuth pectin along with levofloxacin and amoxicillin (EBLA), or esomeprazole along levofloxacin and amoxicillin (ELA) for one week. The primary outcome was the eradication rate in the intention-to-treat (ITT) and per-protocol (PP) analyses.
**Results:** Overall, 270 patients were randomized. The eradication rates in the above three groups were 80.25%, 89.66% and 81.93% in PP analysis and 72.22%, 86.66% and 75.56% in ITT analysis, respectively. The eradication rate of EBLA was significantly higher than that of EBCA (P = 0.016) in ITT analysis. No significant differences were found among these groups in terms of adverse effects and compliance. The efficacy was significantly affected by levofloxacin resistance for EBLA (P = 0.01) and ELA (P = 0.04), but not by polymorphisms of CYP2C19 gene for any of the three groups.
**Conclusion:** One-week bismuth-containing quadruple therapies and levofloxacin-based triple therapy can all obtain an acceptable eradication rate and levofloxacin-based quadruple regimen exhibits the highest eradication rate. The antibiotic resistant rate of levofloxacin was associated with the eradication rate.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1607 ESOMEPRAZOLE BASED TRIPLE THERAPY REGIMENS (EAC/EAM) ON H.PYLORI ERADICATION THERAPY SHOWED HIGH SUCCESS RATE EVEN IF ON EM OF CYP2C19 POLYMORPHISM OR CAM RESISTANCE

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**Introduction:** Success or failure of *H. pylori* (HP) eradication mainly depends on sensitivity of antibiotics for HP and drug adherence of patients. So far now, several proton pomp inhibitors (PPIs) have been used in eradication, most of

reports said that success rate of eradication approximated from 70 to 80% on Amoxicillin (AMX) and Clarithromycin (CAM) based triple therapy in Japan. Recently the ratio of CAM resistance in Japan comes up to over 30%, we have to overcome CAM resistance using any contrivance. On the other hand, recently the stability of continuous gastric acid suppression with PPIs is one of most important factors. At the point of gastric acid suppression, we expect one of strong PPIs Esomeprazol (EPZ).

**Aims & Methods:** The aim of this study is to elucidate effects of drug sensitivity test for HP and CYP2C19 polymorphism on EPZ based triple therapy regimens (EAC/EAM).

This study is a single-center, prospective case study at Heiwadai clinic, Nerima-ku Tokyo, Japan during 15 months from June. 2013 to Aug. 2014. The 167 patients had made entry, and a total of 76 patients (HP positive) were enrolled (26 men and 50 women). Mean age of patients was 57.9 years old. Fisher's exact test was used in all statistical analyses. Regimen of EAC (1st eradication) was EPZ (40) b.i.d., AMX (1.500) b.i.d. plus CAM (400) b.i.d. for 7 days. Regimen of EAM (2nd eradication) was EPZ (40) b.i.d., AMX (1.500) b.i.d. plus MNZ (500) b.i.d. for 7 days. Diagnosis of HP infection was done with rapid urease test and cultivation of HP on EGD. Drug sensitivity test for HP about CAM and MNZ were done with biopsy samples.

**Results:** Success rate of 1st eradication is ITT = 73.6% (56/76) and PPT = 74.7% (56/75). Success rate of 2nd eradication ITT = 100% (17/17) and PPT = 100% (17/17). Resistance of CAM was 30.4% (17/56) and MNZ was 0% (0/17). CYP2C19 polymorphisms were as follows EM: extensive metabolizer 81.6% (62/76), Homo (1/1) 37.1% (23/62), Hetero (1/2, 1/3) 62.9% (39/62) and PM: poor metabolizer 18.4% (14/76). Even if in the cases of CAM resistance, EAC regimen showed relatively higher success rate (64.5%) rather than previous success rate (about 30%) on other PPIs based regimens as 1st eradication. And also EAC regimen showed significantly high eradication rate (90.6%), even if on EM in the cases of CAM sensitive. In particular, EAC regimen showed significantly high eradication rate (100%), on homo-EM in the cases of CAM sensitive. In addition, EAM regimen showed very high success rate (100%) on 2nd eradication.

**Conclusion:** EPZ-based triple therapy regimens (EAC/EAM) on HP eradication showed high success rate even if on EM of CYP2C19 polymorphism or CAM resistance. And also these regimens showed relatively higher success rate rather than previous success rate on other PPIs based regimens.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 09:00–14:00

## SMALL INTESTINAL III – POSTER EXHIBITION

### P1608 THE CLINICAL AND PHENOTYPIC ASSESSMENT OF SERONEGATIVE VILLOUS ATROPHY; A PROSPECTIVE UK CENTRE EXPERIENCE EVALUATING 200 CASES OVER A 15-YEAR PERIOD (2000–2015)

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**Introduction:** Seronegative villous atrophy (SNVA) occurs in 6–22% of coeliac cases. However, there are other causes of SNVA. More recently angiotensin-2-receptor-blockers have been reported as an association but data on SNVA has been limited to centres evaluating complex case referrals and not SNVA in general.

**Aims & Methods:** We aimed to provide clinical outcomes and associations in the largest prospective study overseeing all newcomers with SNVA.

Over a 15-year period (2000–2015) we evaluated 200 adult patients with SNVA at a UK secondary/tertiary-care centre. A diagnosis of either seronegative celiac disease (SNCD) or SN-non-CD was reached. Baseline comparisons were made between the groups, with 343 seropositive CD subjects serving as controls.

**Results:** Of the 200 SNVA cases, SNCD represented 31% (n = 62) and SN-non-CD 69% (n = 138). The HLA-DQ2/8 genotype was present in 61%, with a 51% positive predictive value for SNCD. The breakdown of identifiable causes in the SN-non-CD group include infections (27%, n = 54), inflammatory/immune-mediated disorders (17.5%, n = 35) and drugs (6.5%, n = 13; two cases related to angiotensin-2-receptor-blockers). However, no cause was found in 18% (n = 36) and of these 72% (n = 26/36) spontaneously normalised duodenal histology whilst consuming a gluten-enriched diet. Following multivariable logistic regression analysis a novel independent factor associated with SN-non-CD was non-Caucasian ethnicity (odds ratio 17.2, p = 0.002); in fact, 66% of non-Caucasians had *Helicobacter pylori* and/or alternate gastrointestinal infections. On immunohistochemistry all villous atrophy groups stained positive for CD8-T-cytotoxic intraepithelial lymphocytes. However, additional CD4-T-helper intraepithelial lymphocytes were occasionally seen in SN-non-CD mimicking the changes associated with refractory CD.

**Conclusion:** Most patients with SNVA do not have celiac disease and hence should not be placed on a gluten-free diet without further investigations. Moreover, a subgroup shows spontaneous histological resolution whilst consuming gluten. The presence of non-Caucasian ethnicity should prompt search for an infective aetiology. The role of phenotyping intraepithelial lymphocytes for diagnostic purposes can potentially be misleading.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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1. DeGaetani M, Tennyson CA, Lebwohl B, et al. Villous atrophy and negative celiac serology: a diagnostic and therapeutic dilemma. *Am J Gastroenterol* 2013; 108(5): 647–653.

### P1609 PREVALENCE OF DYSBIOSIS AND EFFECT OF LOW FODMAP DIET IN CELIAC DISEASE PATIENTS WITH IBS-LIKE SYMPTOMS

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**Introduction:** A subgroup of celiac disease patients have IBS (irritable bowel syndrome)-like symtoms despite following a gluten free diet (GFD). It is unknown whether the microbiota in these patients differs from an IBS- and a healthy population, and whether it changes during diet interventions.

**Aims & Methods:** To study the microbiota profile in patients with celiac disease patients and any change with diet intervention to improve symptoms. 40 celiac disease patients with IBS-like symptoms confirmed by the Rome III-criteria and IBS-SSS (symptom severity scale) were compared to Norwegian IBS and healthy cohorts, and randomized as follows: Group A had a more strict GFD for 6 weeks, whilst patients in group B reduced FODMAPs in their GFD. Faecal samples at baseline and 6 weeks. IBS-SSS at BL, 3 and 6 weeks. The faecal samples were analysed by the GA-Map Method (Genetic Analysis AS) for bacteria and Dysbiosis Index (DI) 1–5, where DI > 2 is clinically relevant. Statistics: T-test, Mann-Whitney U, Fisher's linear discriminant analysis.

**Results:** FODMAP intake was reduced from 12 g to 2 g/day (p = 0.0001) in group B only and IBS-SSS improved in both groups. 45% of the patients had dysbiosis at baseline, compared to 73% in an IBS cohort (p < 0.0091) and 16% in healthy controls (p < 0.0007), with a mean score of 2.5 ± 1.1 vs. 3.0 ± 1.0 and 1.7 ± 0.7, respectively. The patients had significantly more Bacilli and Prevotella than healthy controls. In group A (18 F/2 M, age 39 ± 15), dysbiosis stayed constant on diet, but more patients had severe dysbiosis (DI > 3), 15% vs. 25% (p = 0.85). In group B (15 F/5 M, age 44 ± 12), fewer patients had dysbiosis after diet, 60% vs. 50% (p = 0.79). Responders to low FODMAP diet had less *Lactobacilli* and *Firmicutes* (*Clostridia*), and more *Atopobium* at baseline.

**Conclusion:** Celiac disease patients with IBS-like symptoms had less severe dysbiosis than an IBS-population, but more than healthy controls. We found that the level of *Lactobacilli*, *Firmicutes* (*Clostridia*) and *Atopobium* predicted response to the low FODMAP diet.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1610 HAPTOGLOBIN-2 GENE EXPRESSION IN CELIAC DISEASE, NON CELIAC GLUTEN SENSITIVITY AND TYPE 1 DIABETIC PATIENTS

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**Introduction:** Haptoglobin (HP) function has long been known as a scavenger for hemoglobin used as a marker for general inflammation before the discovery of C-reactive protein (Asleh et al. 2003). Human HP appears in three different genotypes: Hp1–1, Hp2–1, and Hp2–2 (Maeda et al. 1984) and many studies have shown association between diseases and the HP phenotype/genotype (Quaye 2008). The HP2–2 phenotype has been associated with worse prognosis of several infectious diseases (Delanghe et al. 1998; Kasvosve et al. 2000), autoimmune disorders such as celiac disease (Tripathi et al. 2009) and neurological disorders (Gloria-Bottini et al. 2008; Maes et al. 2001). Recently, our group has discovered the precursor of haptoglobin-2 (pHP2) is active as zonulin (Tripathi et al. 2009). Zonulin is a protein able to regulate intestinal permeability by reversible disassembly of intercellular tight junctions and has been associated with some autoimmune disorders, diseases of the nervous system, and neoplastic conditions (Fasano 2011). Therefore, our hypothesis is that people with one or two copies of HP2 gene (HP2–1 or HP2–2 genotype) produce more zonulin leading to increased intestinal permeability and will develop a more severe clinical outcome.

**Aims & Methods:** To determine the genotype/phenotype distribution of haptoglobin in celiac disease (CD), non-celiac gluten sensitivity (NCGS), type 1 diabetes (T1D) and first degree relatives of T1D (T1DR). Material and Methods: Samples were obtained retrospectively using biorepository material. HP genotype were done with specific primers designed in exon 2 and exon 5 of HP1 corresponding to exons 2 and 7 of HP2 amplified by high fidelity PCR system. After PCR the amplicons were run on a 1% agarose gel and read under a UV bulb. The

size difference allowed differentiation of the two genotypes (HP1: 2.5 kb and HP2: 5.3 kb). When blood was not available, serum were used to phenotype the individuals by western blot. Serum total proteins were denaturated, separated by size in an electrophoresis gel and then transferred to a PVDF membrane. Imnunoblotting were performed using an anti-zonulin antibody.
**Results:** 1210 individuals were genotyped or phenotyped. HP distribution was statistical different ($p < 0.01$) in all analyzed population comparing to control group ($n = 99$) which frequency was 20.2, 51.5 and 28.3% for HP1–1, HP2–1 and HP2–2 respectively. We observed a decrease in HP1–1 frequency (NCGS 10.6, CD 13.4, T1D 41.3 and T1DR 16.3) and an increase in HP2–2 frequency (NCGS 47.1, CD 44.6, T1D 38.4 and T1DR 43.2).
**Conclusion:** Our data reported for the first time an increased frequency of HP2 gene among celiac disease, NCGS, T1D and first degree relatives of T1D individuals. Interestingly, NCGS showed a higher frequency of HP 2–2 compared to the other diseases that could play a role in the pathogenesis of this controversial clinical entity.
**Disclosure of Interest:** A. Fasano: Stock Holder Alba Therapeutics
All other authors have declared no conflicts of interest.

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### P1611 BONE MINERAL DENSITY PREDICTS DUODENAL MUCOSAL HEALING IN ADULT PATIENTS WITH CELIAC DISEASE ON GLUTEN-FREE DIET


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**Introduction:** A long-term impairment of bone mineral density (BMD) is frequent in some otherwise healthy CD patients on GFD. The normalization of intestinal mucosa is still difficult to predict.
**Aims & Methods:** To investigate the role of dual-energy X-ray absorptiometry (DXA) scan to assess duodenal mucosal healing (DMH) in patients with celiac disease (CD) on a gluten-free diet (GFD). Sixty-four consecutive CD adult patients (18 male and 46 female; median age 36 years, range 18–69) on GFD and with negative CD-related serology were recruited. Clinical features of patients and calcium balance were investigated. After a median period of 6 year GFD (range 2–33 years), patients underwent repeat duodenal biopsy and DXA scan to assess BMD. Data were analysed using unpaired Student's t-test and chi-square or Fisher's exact test as required. A multivariate logistic regression analysis (SPSS Statistic 16.0; IBM, Armonk, NY, USA) was performed. A level of $p < 0.05$ was considered statistically significant.
**Results:** Twenty-four patients (38%) displayed normal BMD and 40 (62%) low BMD, 47 (73%) DMH and 17 (27%) duodenal mucosal lesions. All patients but one with normal BMD (23 of 24, 96%) showed DMH, while among those with low BMD 24 did (60%) and 16 did not (40%) show DMH. At multivariate analysis, being older (OR 1.1, 95% CI 1.03–1.18) and having CD diagnosed at an older age (OR 1.09, 95% CI 1.03–1.16) were associated with low BMD; in turn, having normal BMD was the only variable independently associated with DMH (OR 17.5, 95% CI 1.6–192).
**Conclusion:** In CD patients, particularly those older and with late onset disease, BMD recovery is not guaranteed, notwithstanding strict adherence to diet and negative serology. In this series, a normal DXA scan identified CD patients with DMH, thus being a potential useful tool to plan endoscopic resampling.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1612 COELIAC DISEASE IN INDIVIDUALS WITH FERTILITY PROBLEMS – A REGIONAL EXPERIENCE


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**Introduction:** Coeliac disease affects at 1 in 100 people in Europe but probably only a quarter of people with the condition are clinically diagnosed. It has already been linked to many autoimmune disorders, anaemia, osteoporosis, neurological disorders, unexplained hypertransaminasaemia and infertility/subfertility. There is, however, conflicting evidence of the association between infertility and coeliac disease.
**Aims & Methods:** We aim to prospectively investigate the prevalence of coeliac disease in a cohort of patients seeking fertility treatment in a regional centre in the UK. Between October 2013 to October 2015, all male and female patients attending a specialist fertility clinic in a regional referral centre serving the South West Wales were offered a screening blood test for coeliac disease using IgA class tTG whilst excluding IgA deficiency. All patients met the National Institute for Clinical Excellence (NICE) Guidelines for the diagnosis of fertility problems. Patients with known coeliac disease will be included in the prevalence calculation. The study was approved and supported financially by ABMU Health Board R&D department
**Results:** Sixty-four patients agreed to participate. 47 (73%) were female and 17 (27%) were male. An elevated IgA anti-tTG level (median 14 U/ml, range 11 U/ml to 64 U/ml) (normal level < 10 U/ml), was detected in 4.7% of patients i.e. 1 of 17 male patients (5.9%) and 2 of 47 female patients (4.3%) had elevated IgA tTG levels. None of the patients approached were known to have coeliac disease and none of the patients with raised IgA tTG were anaemic (median Hb 144; range 140 – 156, compared to median 138 and range 112 – 172 for patients with normal IgA tTG) or known to have associated conditions.
**Conclusion:** In the preliminary data, there is an increased prevalence of a positive screening test for coeliac disease among the male (4.7%) and female (5.9%) cohorts of patients with fertility problem as compared to the known prevalence for the general population (1%) (1). The prospective study is ongoing and if the prevalence is confirmed on a larger cohort, it is recommended that a coeliac screen should form part of the basic tests for the investigation of infertility.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1613 OVERWEIGHT STATUS AT DIAGNOSIS OF CELIAC DISEASE IN ADULTS INCREASES RISK FOR METABOLIC SYNDROME AFTER GLUTEN EXCLUSION


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**Introduction:** Metabolic syndrome (MetS) has been previously reported in celiac disease (CD) patients both at presentation and as a result of a gluten-free diet (GFD). Both inflammatory response to gluten ingestion and dietary factors coupled with an improved intestinal absorption after GFD have been previously put forth as potential causes of metabolic imbalance. Evidence to support causal hypotheses are lacking and data regarding prevalence and response to GFD are conflicting.
**Aims & Methods:** The aims of this study were to evaluate the prevalence of MetS at CD presentation, assess response to GFD and identify potential subgroups at risk. We included consecutive adult anti-tTG positive, biopsy proven celiacs. MetS was defined according to the Harmonized criteria[1], after assessing abdominal circumference (AC), arterial pressure, high-density lipoprotein cholesterol (HDL), triglyceride (TGL) and blood glucose titers.
**Results:** We evaluated 81 celiac adults (mean age = 38.1 ± 14.3 years, F/M = 5:1) at diagnosis and after GFD (mean duration 3.6 ± 1.8 years). Histology was graded according to the Corazza-Villanacci classification (Grade A = 10.1%, B = 53.7%, C = 36.2%). Mean anti-tTG levels at onset were 67.1 ± 18.9 vs 4.5 ± 2.2U/dl after GFD. MetS, defined as presence of any 3 out of the 5 criteria, was present at diagnosis in 27.4% of cases, and overall it was not influenced by GFD (25.7%). No difference was observed also for TGL and systolic pressure values. On the contrary, AC (80.8 ± 9.7 vs 83 ± 10.6 cm, $p < 0.001$) and HDL (50.7 ± 13.7 vs 55.9 ± 12.6 mg/dl, $p = 0.007$) increased, while blood glucose (92.4 ± 9.9 vs 87.6 ± 9.7 mg/dl, $p = 0.04$) and diastolic pressure (75.7 ± 12.5 vs 70.7 ± 9.7 mmHg, $p = 0.001$) improved. Baseline BMI did not correlate to MetS at CD diagnosis. However, after GFD, subjects with MetS presented a higher BMI when compared to non-MetS (25.5 ± 4.1 vs 20.9 ± 2.9, $p = 0.001$). Furthermore, subjects overweight at diagnosis showed a relative risk of 4.82 (95%CI: 2.08–11.18) for MetS after GFD when confronted with normal/underweight patients (MetS prevalence after GFD 64.3% vs 13.3% respectively, odds ratio 11.7, $p < 0.001$). Age but not sex or atrophy correlated with MetS both at diagnosis and after GFD.
**Conclusion:** Met-S prevalence in adult celiacs in our sample was comparable to previously reported figures for the general population[2]. We also noted no difference in overall prevalence after GFD, contrary to previous studies reporting variably higher or lower prevalence[3,4]. Uniquely, we detected an almost 5-fold relative risk for MetS after GFD in patients who were overweight at CD diagnosis, with a corresponding 125% increase of MetS prevalence in this subgroup. While the inflammatory nature of the active CD has been suggested as the cause of MetS in a malabsorptive syndrome, our data show that arguably milder phenotypes such as overweight patients, are more at risk after dietary intervention.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1614 PREVALENCE OF CELIAC DISEASE AMONG SYMPTOMATIC PATIENTS IN KUWAIT; A POPULATION BASED RETROSPECTIVE COHORT STUDY

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**Introduction:** Celiac disease has a prevalence of 1:70 to 1:300 in most countries (1). Population based studies using serological screeingn with biopsy verification improved our understanding of Celiac disease epidemiology. Data about Celiac disease in the Middle East reigon specially in Kuwait are limited.
**Aims & Methods:** We aimed at estimating the prevalence of Celiac disease among symptomatic patients in Kuwait. We retrospectively analyzed data of 1954 consecutive patients who had symptoms justifying testing for Celiac serology between 2010 and 2015. They were subjected to Celiac serology testing (either human tissue transglutaminase antibody or anti-endomysial antibody). Patients who had at least one positive Celiac serology were subjected also to endoscopy and duodenal biopsy to confirm diagnosis of Celiac disease. Celiac disease diagnosis was based upon concordance between serology and histopathology.
**Results:** A total of 1954 patients were referred for Celiac serology testing; 182 (9.3%) were having positive Celiac serology. Among those 182 patients; 91 (50%) were Kuwaitis and 91 (50%) were non- Kuwaitis; 60 (33%) were males and 122 (67%) were females. Diagnosis of Celiac disease was confirmed by endoscopy and duodenal biopsies in 50 (2.55%) patients. Diagnosis of Celiac disease was more common in non-Kuwaiti than Kuwaiti and in females more than males.
**Conclusion:** Celiac disease can be an underestimated problem in symptomatic Kuwaiti and non-Kuwaiti patients. Larger population based studies are warranted to accurately estimates prevalence of celiac disease in Kuwait.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1615 NATIONWIDE POPULATION-BASED COHORT STUDY OF CELIAC DISEASE AND RISK OF EHLER–DANLOS SYNDROME AND JOINT HYPERMOBILITY SYNDROME

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**Introduction:** Patients with celiac disease (CD) often have articular complaints, and small prior studies suggest an association with Ehler-Danlos Syndrome (EDS) and Joint Hypermobility Syndrome (JHS).
**Aims & Methods:** This cohort study compared all individuals in Sweden diagnosed with CD based on small intestinal biopsy between 1969–2008 (n = 28.631) to 139,832 matched reference individuals, and to a second reference group undergoing biopsy without having CD (n = 16.104). Rates of EDS/JHS were determined based on diagnostic codes in the Swedish Patient Register. Hazard ratios (HRs) for EDS/JHS were estimated through Cox regression.
**Results:** There were 45 and 148 cases of EDS/JHS in patients with CD and reference individuals, respectively. This corresponds to a 49% increased risk of EDS/JHS in CD (95%CI = 1.07–2.07). The HR for EDS was 2.43 (95%CI = 1.20–4.91) and for JHS 1.34 (95%CI = 0.93–1.95). Compared to reference individuals undergoing intestinal biopsy, CD was not a risk factor for EDS/JHS. A stronger association was seen in patients initially diagnosed with EDS/JHS and subsequently diagnosed with CD (Odds Ratio = 2.29; 95%CI = 1.21–4.34).
**Conclusion:** Individuals with CD have higher risk of EDS/JHS than the general population, which may be due to surveillance bias or factors intrinsic to celiac development.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1616 USEFULNESS OF CAPSULE ENDOSCOPY IN CELIAC DISEASE: A EUROPEAN MULTICENTER STUDY

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**Introduction:** Capsule endoscopy (CE) may play a role in coeliac disease (CD).
**Aims & Methods:** Retrospective multicenter observational study. Two-hundred and fifty-eight patients (mean age: 46.5 ± 16.9 years, 31% men) who underwent a CE from 2003 to 2016 at 14 European centres were included. They were classified in Group A (equivocal diagnosis, n = 80) and Group B (nonresponsive CD and/or persisting symptoms, n = 178). Baseline characteristics, serology and HLA typing were collected. Diagnostic yield was defined as endoscopic markers of CD or other enteropathy. Clinical impact of CE and patient outcome were also assessed.
**Results:** Patients with antibody-negative villous atrophy (Group A1, n = 18, 7%) achieved an 83.3% diagnostic yield. Gluten-free diet was successfully indicated in 7 of 9 cases (77.78%). Among the Marsh I-II patients (Group A2, n = 57, 22.1%), there were cases with a positive serology (n = 17, 29.8%), and a positive HLA (n = 23, 40.3%). Diagnostic yield was 61.4%, identifying diffuse or patchy CD atrophy (n = 26, 45.6%) and complicated CD (n = 6, 10.5%). Considering patients refusing conventional gastroscopy (Group A3, n = 5, 2%), there were 4 (80%) diagnosed of CD by CE. CE achieved a 64.7% diagnostic yield within coeliac patients (Group B, n = 178, 69%). Twenty jejunoileitis (11.2%) and 7 lymphomas (3.9%) were detected. The diagnostic yield of CE in Group A was not statistically different than that of CE in Group B (66.3% vs. 65.7% respectively, p = 0.935). Globally, CE (mean small bowel time: 259.5 ± 97.5 min) achieved a 65.7% clinical impact. This device has modified the diet (n = 82, 49.1%, with a positive response in 81.7%), indicated new procedures (n = 58, 34.7%, with 33 balloon-assisted enteroscopies), new drugs (n = 25, 15%) and surgery (n = 3, 1.8%). Other inflammatory enteropathies were diagnosed in 13 cases (5%, 7 patients with Crohn's disease). There were no complications related to CE.
**Conclusion:** CE may have a high diagnostic yield and modify the outcome of patients with CD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1617 HOW MUCH GLUTEN IS THE GENERAL POPULATION CONSUMING AND DOES IT RELATE TO SYMPTOMS?

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**Introduction:** Gluten is a ubiquitous part of a Western diet. It is implicated for causing an array of disorders, which have both intestinal and/or extraintestinal manifestations. Our understanding of this heterogeneous group of gluten-related disorders is advancing, however uncertainty exists as to how much gluten the general population is consuming. This study aims to address this knowledge gap and also assess the prevalence of self-reported gluten sensitivity within the general population.
**Aims & Methods:** Between September and October 2015 a population-based survey was undertaken in Sheffield, UK. Members of the general public, all over the age of 16 years, were invited to complete a modified version of a previously validated written questionnaire. This questionnaire assessed demographic information, GI conditions and also determined the presence of gluten sensitivity (GS). In addition, total gluten consumption was calculated using a food frequency questionnaire. Participants were asked about their use of a gluten-free diet (GFD), and whether they had seen a healthcare professional for their symptoms. A diagnosis of coeliac disease (CD) was determined if individuals had a doctor diagnosis of CD, and were also taking a GFD.
**Results:** 1003 adults completed the population-based survey (59% female, median age 31 years (16–86years). The mean consumption of gluten per day for this group was 13.2 g (s.d = 9.2 g). The self-reported prevalence of GS was

32.5% (326/1003, female 70% [$P < 0.0001$], age range 17–82, median age 35yrs), with 3.7% (38/1003) on a GFD and 1.1% (12/1003) having CD. The proportion of GS individuals who had seen a doctor for their symptoms was 18.3% (65/326). Individuals with GS had an increased prevalence of fulfilling the Rome III criteria for irritable bowel syndrome, in comparison with those without GS (31.3% vs. 5.61%, odds ratio 7.66, $p < 0.0001$). In addition, mean daily consumption of gluten was considerably lower in this GS group compared to the non GS group (10.8 g vs. 14.4 g, $p < 0.0001$).
**Conclusion:** This is the first study assessing gluten consumption in a UK population. Findings from our work highlight that sensitivity to gluten-based products is common, and that affected individuals have a higher prevalence of IBS. Although only a minority of individuals maintained a GFD, individuals with gluten-related symptoms evidently were electing to reduce their gluten consumption.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1618 A SELF-ADMINISTERED BLIND GLUTEN CHALLENGE ASSOCIATED TO AN ANDROID/IOS APPLICATION (TEST33®) TO DIAGNOSE NON-CELIAC GLUTEN SENSITIVITY

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**Introduction:** Non-celiac gluten sensitivity (NCGS) is a syndrome characterized by the quick onset of intestinal and/or extraintestinal symptoms after the ingestion of gluten containing food, in absence of celiac disease and wheat allergy. International Guidelines indicate blind gluten challenge as the unique diagnostic test for NCGS. Test33® is a commercially available kit incorporating a blind gluten challenge.
**Aims & Methods:** Our aim was to evaluate the efficacy of Test33® in NCGS diagnosis and gluten-related symptoms Test33™ is a commercially available kit containing undistinguishable gluten and placebo capsules identifiable through a unique code. The kit is integrated by an application (app). Patient downloads the app on him/her smartphone or tablets (Ios or android) and it guides him/her through the administration of the capsules, their sequence and evaluation of symptoms by means of 33 10-cm long VASs on the screen of their devices. 10 VASs evaluated gastrointestinal symptoms and 23 VASs extraintestinal ones. After a three-week-long gluten-free diet (GFD), responsive patients (indicated by the app) were randomly assigned to gluten intake (5.6 g/day) or placebo for seven days, followed by washout and crossover (one week each). The challenge is self-administered at home by the patient who previously excluded celiac disease and wheat allergy. The primary endpoint was the worsening of symptoms (VAS increase $\geq 3$ cm) during gluten ingestion compared to placebo to define NCGS.
**Results:** 69 patients (55 females, $38 \pm 18$ years of age) made the test and 61 (88%) completed the challenge and symptomatic VASs. In 93% of cases VASs values significantly improved after GFD. During the blind challenge none of the symptoms worsened during placebo assumption phase. On the contrary, among gastrointestinal symptoms, abdominal pain, constipation, meteorism and bloating resulted significantly worsened by blind gluten ingestion compared to placebo ($3.1 \pm 3.0$ vs $2.2 \pm 2.0$, $3.3 \pm 3.0$ vs $2.4 \pm 2.7$, $4.9 \pm 3.5$ vs $3.8 \pm 3.2$, $4.2 \pm 3.0$ vs $2.8 \pm 3.0$, respectively); among extraintestinal symptoms, joint and muscolar pain were significantly worsened by blind gluten ingestion compared to placebo ($3.3 \pm 3.3$ vs $2.5 \pm 3.0$ and $2.8 \pm 2.6$ vs $1.9 \pm 2.0$, respectively). Six females out of 61 subjects (6%, $31 \pm 16$ years old) satisfied critera for NCGS diagnosis. In these patients 13 (39%) VAS values significantly worsened after gluten ingestion compared to the 6 (18%) altered by gluten in the whole cohort of patients.
**Conclusion:** The self-administered blind gluten challenge supported by a dedicated app (Test33®) effectively evidenced NCGS patients among suspected individuals. Moreover, it evidenced those symptoms (intestinal and extraintestinal) strictly correlated to the blind gluten ingestion.
**Disclosure of Interest:** L. Elli: Coinventor of Test33
L. Roncoroni: Coinventor of Test33
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A. Catania: Head of Prodecopharma
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## P1619 PREDICTORS OF RESPONSE TO TEDUGLUTIDE AMONG PATIENTS WITH PARENTERAL NUTRITION-DEPENDENT SHORT BOWEL SYNDROME

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**Introduction:** The study aimed to identify factors associated with sustained parenteral nutrition (PN) volume reduction and early vs. late responders among PN-dependent short bowel syndrome patients treated with teduglutide (TED).
**Aims & Methods:** The study population was 43 patients receiving TED in a 24-week randomized placebo-controlled trial (STEPS: NCT00798967; EudraCT2008–006193-15) who could continue TED up to 24 months in the open-label extension (STEPS-2: NCT00930644; EudraCT2009–011679-65). Time to sustained PN volume reduction (i.e., PN volume reduction $\geq$20% at 2 consecutive visits) was calculated using Kaplan-Meier analysis. Multivariable Cox model was used to identify factors associated with sustained PN volume reduction. Among patients achieving sustained PN volume reduction, baseline characteristics were compared between early (PN volume reduction $\geq$20% at week 20 and 24) vs. late responders (sustained PN volume reduction at 2 consecutive visits after week 24).
**Results:** The median time to sustained PN volume reduction was 4.2 months. Patients with stoma, compared to those without, were significantly more likely to achieve sustained PN volume reduction (HR=5.6; $P = 0.01$). Patients with an ileocecal valve, compared to those without ($HR = 0.1$; $P = 0.03$), and patients with major intestinal resection due to vascular disease, compared to those with Crohn's disease ($HR = 0.2$; $P = 0.02$), were significantly less likely to achieve sustained PN volume reduction. Compared to late responders ($n = 7$), early responders ($n = 27$) were less likely to have colon-in-continuity (52% vs. 100%; $P = 0.02$) and ileocecal valve (0% vs. 29%; $P < 0.01$), and had smaller mean percentage of colon remaining (25% vs. 57%; $P = 0.02$). The median time to sustained PN volume reduction was 3.7 months for early responders and 7.8 months for late responders.
**Conclusion:** Presence of stoma and absence of ileocaecal valve are good prognosis factors for achieving sustained PN volume reduction while vascular disease as cause of intestinal resection is a negative prognosis factor. Certain anatomical factors were significantly different between early and late responders.
**Disclosure of Interest:** F. Joly: Served a study investigator for NPS Pharmaceuticals, Inc and advisory board member for Fresenius, Baxter Healthcare, Nestlé Health Sciences, Homeperf and Aguettant
S.M. Gabe: Served as an advisory board member and study investigator for NPS Pharmaceuticals, Inc., as an advisory board member for Medtronic and lecturer for Baxter and BBraun.
D.L. Seidner: Served as an advisory board member and study investigator for NPS Pharmaceuticals, Inc., and as a consultant for Fresenius Kabi and Option Care
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S.S. Kelkar: Employee of Analysis Group which received payment from Shire plc for research analysis
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## P1620 LACTOSE MALABSORPTION IN SUBJECTS WITH SELF-PERCEIVED MILK INTOLERANCE ASSESSED WITH THE ROMA III QUESTIONNAIRE FOR IBS

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**Introduction:** Lactose malabsorption is a common condition with symptoms similar to those in functional disorders. IBS patients often attribute their symptoms to the intake of food, particularly milk and dairy products. Lactose hydrogen breath test (HBT) is the method of choice to identify lactose malabsorption and this test is increasingly prescribed by primary care physicians and gastroenterologists in patients reporting milk intolerance.
**Aims & Methods:** The aim of this study was to determine in a cohort of patients with self-perceived lactose intolerance whether a preliminary assessment with the Rome III questionnaire for IBS was able to discriminate patients with lactose malabsorption from those with functional disorders only.396 consecutive patients (90 M, 272 F, median age 38, range 18–78) with self-perceived milk intolerance and referred to our Unit for a lactose HBT by a general practitioner or a gastroenterologist were studied. After an oral challenge with 20 g of lactose, end-expiratory breath samples were collected before and at 30 min intervals for 3 hours. A positive test was defined as an increase in hydrogen above basal levels greater than 20 ppm and defined lactose malabsorption. All patients

underwent anti-tissue transglutaminase (anti-tTG), total IgA assay and completed the Rome III questionnaire before performing HBT.
**Results:** Thirty-four patients (8.5%) were anti-tTG positive with normal IgA and celiac disease diagnosis was confirmed by histology. A total of 245 (67.6%) patients were diagnosed as having IBS, including 67 (27.3%) with diarrhea (IBS-D), 30 (12.2%) with constipation (IBS-C), 73 (29.7%) alternating diarrhea and constipation (IBS-M) and 75 (30.6%) unclassified (IBS-U). A positive HBT was found in 105 (42.8%) patients with IBS and in 53 (45.2%) patients among those who did not fulfilled Rome III criteria ($p = 0.5$). No differences among subgroups identified by the Rome III criteria and between patients referred by either a primary care physician or gastroenterologist were found.
**Conclusion:** Lactose malabsorption has a similar prevalence in patients with and without IBS. The Rome III diagnostic questionnaire failed to discriminate subjects with lactose malabsorption among patients with subjective perception of milk intolerance. In these patients, the completion of the Rome III questionnaire for IBS before performing a lactose HBT is not justified in the daily practice.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1621 POST HOC ANALYSIS OF POLYPS IN 9 SHORT BOWEL SYNDROME PATIENTS TREATED WITH TEDUGLUTIDE

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**Introduction:** Preclinical data raise the possibility that teduglutide may be associated with a risk of small intestinal and/or colonic neoplasia.
**Aims & Methods:** This report aims to evaluate data from 2 clinical trials in patients with short bowel syndrome (SBS) who reported polyps at baseline or during long-term teduglutide treatment. Post hoc analysis of data was reported in patient e-case forms (eCRFs) regarding gastrointestinal polyps at baseline and over the course of 2 therapeutic trials of teduglutide (STEPS: NCT00798967, EudraCT2008–006193-15; STEPS-2: NCT00930644, EudraCT2009–011679-65). A baseline colonoscopy was required unless a normal colonoscopy had been performed $<6$ months before screening. Patients with benign polyps removed prerandomisation were eligible for enrolment.
**Results:** Of the patients enrolled (STEPS, $n = 86$; STEPS-2, $n = 88$), 54 who had not undergone prior colectomy received a baseline colonoscopy and 50 received a study completion colonoscopy (remaining patients refused or no colon was present). Baseline colonic polyps were reported in 9 patients (ages 39–75 years; women, 67%); per inclusion criteria they were removed before treatment initiation. By the end of STEPS-2, 9 patients (ages 35–63 years; women, 67%) had reported polyps. In 6 of these 9 patients, polyps were recorded as a treatment-emergent adverse event (TEAE). Patients had been on teduglutide for 3 months (1 patient, TEAE), 8 months (1 patient, TEAE), 10 months (1 patient, TEAE), 24 months (5 patients, 3 TEAE) and 30 months (1 patient, 0 TEAE) at polyp detection. Polyp locations were colon (7 patients), duodenum (1 patient), and unknown (1 patient). Recorded polyp sizes were 2–7 mm (4 patients). 7 patient eCRFs noted that biopsies were performed; 2 recorded low-grade dysplasia (rectal/colorectal polyps), but none recorded overt malignancy.
**Conclusion:** Polyps were reported in 9 of 50 patients receiving long-term teduglutide who had a colonoscopy at study completion (106.3 patient-years exposure). There were no reports of malignancy related to the presence of these polyps. Additional information regarding polyp incidence will be acquired from an ongoing SBS registry.
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S. Rudzki: Has served as a study investigator for NPS Pharmaceuticals, Inc.
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## P1622 THE UTILITY OF SMALL INTESTINE CAPSULE ENDOSCOPY AND BALLOON-ASSISTED ENTEROSCOPY IN THE DIAGNOSIS OF SMALL INTESTINAL TUMORS

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**Introduction:** Both small intestine capsule endoscopy (SCE) and balloon-assisted enteroscopy (BAE) play an important role in the diagnosis of small intestinal tumors. However, the usefulness of both modalities is still unclear. To confirm their utility and diagnostic ability, we aimed to examine cases of small intestinal tumors diagnosed using SCE and BAE at our institute, and compare them with those diagnosed using computed tomography (CT) or magnetic resonance imaging (MRI).
**Aims & Methods:** Between April 2008 and March 2016, 668 and 507 patients underwent BAE and SCE, respectively, at our institute. Of these, 59 (34 men and 25 women; median age, 62 years) were confirmed as having small intestinal tumors and were included in this study to determine the usefulness of the aforementioned diagnostic modalities for small intestinal tumors. The utility of CT, MRI, SCE, and BAE was investigated and retrospectively compared for all the cases.
**Results:** No adverse effects were observed for any modality. The chief complaints were unidentified anemia/obscure gastrointestinal bleeding (17 cases, 29%); suspicion of tumor based on the results of other diagnostic modalities, without abdominal symptoms (16 cases, 27%); and abdominal symptoms (12 cases, 20%). The final diagnoses of the 59 cases were small intestinal cancer (15 cases, 29.6% [10 primary/5 metastases]), non-epithelial tumor (15 cases, 25.5%), malignant lymphoma (14 cases, 24.7%), and hereditary polyposis (12 cases, 20.3%). BAE was performed for all the cases, and SCE was performed for 28 of the 59 cases. CT/MRI was performed for 57 cases, excluding 2 cases with Peutz-Jeghers syndrome. In 19 (32.2%) of the 59 cases, the tumor was not detected by CT/MRI. These cases were non-epithelial tumors (7 cases, 36.8%), hereditary polyposis (6 cases, 31.6%), small intestinal cancer (3 cases, 15.8% [2 primary/1 metastasis]), and malignant lymphoma (3 cases, 15.8%). BAE detected the tumor in 19 cases, and SCE was performed in 13 of these 19 cases. Four (30.8%) of the 13 cases were not detected as small intestinal tumors but as malignant lymphoma in 1 case and non-epithelial tumor in 3 cases. By using SCE and/or BAE, even cases that were not detected on CT/MRI as small intestinal tumors because of their small size and slight mucosal changes were detected.
**Conclusion:** For patients with suspected small intestinal tumors, imaging modalities for the small intestine are useful for diagnosis. However, in some cases, small intestinal tumors are difficult to detect by CT/MRI studies because of their size and mucosal changes. For cases that are strongly suspected to be small intestinal tumors, performing SCE and/or BAE should be considered, even when no lesions are detected by CT/MRI.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1623 DOUBLE BALLOON ENTEROSCOPY IN SMALL BOWEL TUMORS: 11 YEARS' EXPERIENCE AT A TERTIARY-CARE HOSPITAL

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**Introduction:** The small bowel tumors prevalence is 3–6%, being 5.5% in Portugal. In our center, the prevalence of malignant small bowel tumors was 9.4% between 2005 and 2008. Double-balloon enteroscopy (DBE) is the gold standard in a suspicion of small bowel tumors.
**Aims & Methods:** We aimed to characterize the small bowel tumors detected by DBE and the diagnostic value of DBE in small bowel tumors. This was a retrospective study of DBE performed between January 2005 and November 2015, which included all patients with a suspected small bowel pathology and negative previous conventional study. Collected clinical, endoscopic, imagiological and surgical data of diagnosed tumors. Evaluation of DBE diagnosis value comparing with Capsule endoscopy and CT enterography.
**Results:** Performed 267 DBE in 213 patients, 55.8% males and mean age of $60.4 \pm 17.8$yo. The main indication for DBE was obscure gastrointestinal bleeding in 62.5%, being occult in 71.9% of cases. Performed 187(70.0%) exams by anterograde route, 73(27.3%) by retrograde route and 7(2.6%) by both routes. Lesions were detected by DBE in 66.3%(177/267) of cases, mainly angioectasias (67/177; 37.8%). Thirty-two small bowel tumors in 30 patients were diagnosed. The diagnosis by DBE was 87.5%(28/32). Biopsies were obtained in 59.4% of tumors with 3 of them negative (15.8%). Most tumors were sub-epithelial lesions (17/32; 53.1%), malignant lesions (19/32; 59.4%) and localized in jejunum (21/32; 65.6%). The main diagnosis of malignant tumors was gastrointestinal stromal tumors in 21.9%(7/32), adenocarcinoma in 15.6%(5/32), lymphoma in 5.8%(3/32) and metastatic tumors in 5.8%(3/32). According to the final diagnosis, DBE showed high diagnostic accuracy (93.4%; $p < 0.001$) comparing with Capsule endoscopy (86.1%; $p < 0.001$) and CT enterography (72.9%; $p = 0.032$).
**Conclusion:** Small bowel tumors diagnosis was 12.0%(32/267) by DBE and malignant in 7.1%(19/267) of exams. DBE is a useful tool with high diagnostic

accuracy in the study of small bowel tumors comparing with CT enterography or capsule endoscopy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1624 RISK FACTORS FOR ADVANCED SMALL BOWEL DISEASE IN FAMILIAL ADENOMATOUS POLYPOSIS: A PROSPECTIVE, SINGLE-CENTER STUDY

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**Introduction:** Prophylactic colectomy in patients with Familial Adenomatous Polyposis (FAP) has risen the importance for defining more effective strategies for small bowel disease prevention and management. Duodenal adenocarcinoma and ampullary carcinoma relative risks in FAP have been estimated 100 to 330 times higher than in general population. Moreover duodenal adenomatosis prevalence varies among different populations across the world. However risk factors that predict advanced small bowel disease have not been clearly established.
**Aims & Methods:** The aim of this study is to determine clinical features associated with the development of advanced duodenal polyposis, jejunal polyposis and ampullary adenomas in a Brazilian population of patients with FAP. This is a single referral center, prospective study of a cohort of 63 patients with clinical and or genetic diagnosis of FAP. All patients were evaluated with lateral and forward view gastroduodenoscopy. Duodenal polyposis was classified according to Spigelman staging system and ampullary adenomas were also identified. Patients graded as Spigelman III or IV underwent double balloon endoscopy (DBE) for jejunal examination.
**Results:** A total of 63 patients from 48 families with FAP were included in this study. Duodenal adenomatosis stage 0-II was detected in 51, 80.95% (22 male/29 female) patients at a mean age of 35.34 years. Advanced duodenal polyposis (Spigelman III or IV) was present in 12, 19.05% (7 male/5 female) patients at a mean age of 37.2 years. There was no statistically significant difference between the severity of duodenal polyposis and age or gender. There were 26 family members related to 11 different families. The familial distribution of duodenal polyposis severity is presented in the table below, showing that there was a correlation of Spigelman score among different first-degree relatives from each family.

| Family | Number of relatives studied | Spigelman score of family members |
|---|---|---|
| 1 | 2 | IV,IV |
| 2 | 2 | IV,IV |
| 3 | 3 | II,II,0 |
| 4 | 3 | I,0,0 |
| 5 | 2 | 0,0 |
| 6 | 2 | II,0 |
| 7 | 2 | II,II |
| 8 | 2 | 0,0 |
| 9 | 4 | II,II,I,0 |
| 10 | 2 | III,II |
| 11 | 2 | III,II |

Minor ampullary adenomas (defined as adenomas less than 10 mm, without villous architecture or high-grade dysplasia) were detected in 6 patients (5 male/1 female) from 6 different families at a median age of 35.33 years. Three patients with ampullary adenomas were graded as Spigelman III, two patients as Spigelman II and one as O. DBE has been performed in 9 cases of duodenal polyposis graded as Spigelman III or IV. Of those, 7 patients presented small tubular adenomas with low-grade dysplasia located in proximal jejunum and 2 had no jejunal polyps.
**Conclusion:** 1. Advanced duodenal polyposis phenotype is predictable upon disease severity of a first-degree relative; 2. Jejunal endoscopic surveillance is advised in patients with Spigelman III/IV duodenal polyposis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1625 ONCOFETAL PROTEIN IMP3 EXPRESSION IN LYMPH NODE METASTASES OF SMALL-INTESTINE NEUROENDOCRINE NEOPLASMS: A NEW PREDICTOR OF RECURRENCE INDEPENDENT OF THE KI-67 INDEX

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**Introduction:** Small-intestine neuroendocrine neoplasms (SINENs) are heterogeneous neoplasms arising from endocrine cells of the intestinal mucosa. Ki-67 is the main determinant of prognosis in NENs. However, the search for new prognostic makers represents a key point with regard to SINENS. The oncofetal protein IMP3 plays a role in cell growth and its expression has a prognostic value in lung neoplasms. To date, though, there have been no studies focusing on IMP3 role in ileal neuroendocrine tumors.
**Aims & Methods:** Our research aimed to investigate whether IMP3 protein can be detected in SINENs and developed as a new clinical tissue prognostic biomarker for these tumors From January 1998 to August 2015, all the consecutive SINEN patients suitable for surgery were included: 51 patients (34 males, median age 68 years) had SINENs. Each neoplasm was classified according to the WHO 2010 classification, based on the Ki-67 index. In all the cases IMP3 expression was evaluated on primary tumors and, when available, on nodal and distant metastases. The medical records and pathological slides of these patients were used to determine the clinical characteristics, pathological diagnoses, and outcome information
**Results:** In present series, 24 patients (47%) had NENs of grade 1 (G1), 5 (10%) had G2 and 22 (43%) had G3 NENs. The overall 5-year and 10-year survival rate was 53.9% and 42% respectively. Overall, IMP3 was was espressed in 32 out of 57 primary tumors (56%), 19 out of 36 nodal metastases (53%) and 12 out of 22 liver metastases (54%). of the patients. At Cox proportional hazards regression grading was the major factor influencing both OS and PFS at univariate ($p = 0.0002$ and 0.005, respectively) and multivariate analysis ($p = 0.0003$ and 0.005, respectively). Also IMP3 expression at the nodal metastases resulted a factor significantly associated with PFS at both univariate ($p = 0.006$) and multivariate analysis ($p = 0.023$, HR 2.39). IMP3 expression did not correlate with the Ki-67 index ($p =$ n.s.) When considering IMP3 expression classified as scores, in the whole series PFS resulted significantly different, with cases with 2+and 1+ scores showing a worse PFS compared to cases with 0 scores ($p = 0.0015$).
**Conclusion:** In this study, IMP3 at the nodal site resulted to be associated with low PFS in SINENs, independently of the Ki-67 index. In SINENs patients the strong association between IMP3 expression in lymph node metastases and the increased risk of recurrence represents new interesting evidence We suggest that the integration of IMP3 and Ki-67 would help better stratify the risk of progression in SINENs.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1626 ENDOSCOPIC CHARACTERIZATION OF GASTROINTESTINAL STROMAL TUMORS OF THE SMALL BOWEL USING DOUBLE-BALLOON ENTEROSCOPY

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**Introduction:** Gastrointestinal stromal tumors (GIST) are mesenchymal neoplasms that arise from the cells of Cajal in the gastrointestinal (GI) tract. While most GISTs are located in the stomach, 30% of GISTs are found in the small bowel. Small-bowel GISTs tend to be more aggressive and have a worse prognosis with a 5-year survival rate for patients with small-bowel malignant GISTs is approximately 25%. Therefore, an early diagnosis is mandatory. Patients with GIST usually present with obscure gastrointestinal bleeding, which results from a surface ulceration and necrosis. However there is a lack of information about the endoscopic characterization of GIST, especially when using deep enteroscopy such as single and double balloon enteroscopy methods.
**Aims & Methods:** The aim of this case study is to describe the endoscopic spectrum of small bowel GISTs. This is an observational, retrospective, consecutive case series of patients with small bowel GIST of patients included in a prospective database. All procedures were performed by one therapeutic endoscopist. The following information was collected: description of all the lesions, pictures, at least 6 biopsies of each case, ocation of the lesion, indication, procedure time, and instruments used, submucosal injection solutions, complications and follow-up.
**Results:** A total of 10 smalll bowel GISTs were found during a three year period (6 male, 4 female). All patients presented with obscure gastrointestinal bleeding (overt, n = 8, occult, n = 2). The mean age of the patients was 52 years (range 28 to 68). Seven patients had a previous capsule endoscopys study, which was negative in three. Most GISTs were present in the proximal or middle small bowel (n = 7). Computed tomography showed a large mesenteric tumor in one patient (with a huge necrotic small bowel tumor). We defined the endoscopic characteristics based on shape and mucosal surface. The endoscopic tumor characteristics could be categorized as follows: submucosal round (n = 4), submucosal sessile (n = 2), and invasive/penetrating) (n = 4). The mucosa overlying the tumor was normal (n = 4), grooved (n = 3) or frankly ulcerated (n = 1). Biopsy was negative in all patients with normal mucosa but showed tumor in all patients with ulcerations. Regardless of biopsy results, all patients were sent for surgery. Nine resections were carried out. One patient refused surgery. There were no complications of endoscopy in this cohort.
**Conclusion:** This is the largest series of small bowel GISTs documented by double balloon enteroscopy. Our series shows that GISTs have a wider spectrum of endoscopic characteristics than previously described. The round type with normal overlying mucosa was equally prevalent as the grooved or ulcerated variant. This is important to know, as capsule endoscopy and traditional enteroscopy with biopsies may be falsely negative. Endosocopist should be aware of this wide spectrum of presentation of small bowel GIST.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 09:00–14:00
**NUTRITION III – POSTER EXHIBITION**

## P1627 THE FIRST PROCEDURELESS GASTRIC BALLOON FOR WEIGHT LOSS: FINAL RESULTS FROM A MULTI-CENTER, PROSPECTIVE STUDY EVALUATING SAFETY, EFFICACY, PARTICIPANT PREFERENCE, AND LONG TERM FOLLOW-UP

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**Introduction:** Traditional gastric balloons for weight loss require endoscopy and anesthesia for placement and removal. Elipse™ (Allurion Technologies, Wellesley, MA USA) is the first procedureless gastric balloon. The balloon is swallowed, resides in the stomach for 4 months, and is then excreted.
**Aims & Methods:** The objectives of this study were to assess the safety of Elipse™ and to measure its short and long-term effects on weight loss, quality of life, and participant preference. Each participant swallowed one Elipse™ device, which was filled with 550 mL of filling fluid through a thin delivery catheter that was then removed. Three different anti-emetic regimens (ondansetron, aprepitant, and ondansetron + aprepitant) were tried throughout the study. Weight and body composition were measured every 2 weeks by bio-impedance during balloon therapy. After balloon passage, weight was measured monthly although there was no dietary counseling provided. Quality of life was assessed at baseline and at trial exit using the Impact of Weight on Quality of Life (IWQoL) questionnaire. At trial exit, participants were asked if they would recommend Elipse™ to a friend or repeat it if they regained weight.
**Results:** Thirty-four participants were enrolled with a mean BMI of 34.8 kg/m$^2$. At 4 months, the mean weight loss was 10.0 kg, percent total body weight loss (%TBL) was 10.0%, and percent excess weight loss (%EWL) was 39%. 100% of the weight lost was from fat. All adverse events were either self-limiting or resolved with medication. Vomiting was significantly reduced using a combination of ondansetron and aprepitant. All balloons were safely excreted. At trial exit, IWQoL scores improved across all domains. In the absence of any post-balloon dietary counseling, 93% and 63% of the weight lost was maintained at 6-month and 9-month follow-up, respectively. 93% and 86% of participants would recommend Elipse™ to a friend or repeat it if they regained weight, respectively.
**Conclusion:** Elipse™ leads to weight loss on par with endoscopic balloons but does so without endoscopy and anesthesia and without sacrificing safety or the participant experience. In addition, in the absence of post-balloon dietary counseling, participants maintained nearly two-thirds of the weight lost during therapy at 9-month follow-up.
**Disclosure of Interest:** R. Chuttani: Shareholder, Allurion Technologies
I. Raftopoulos: Consulting Fees, Allurion Technologies
K. Stecco: Consulting Fees, Allurion Technologies
S. Levy: Shareholder, Allurion Technologies
S. Gaur: Shareholder, Allurion Technologies
E. Machytka: Consulting fees, Allurion Technologies
All other authors have declared no conflicts of interest.

## P1628 CHILD WEIGHT STATUS INFLUENCES THE IMPROVEMENT IN INSULIN SENSITIVITY FOLLOWING A SHORT-TERM ENERGY RESTRICTION IN SEVERELY OBESE PATIENTS

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**Introduction:** Ectopic lipid accumulation is a common factor underlying non-alcoholic fatty liver disease (NAFLD) and Type 2 diabetes (DM). Adipose tissue capacity that is fixed in adolescence and overwhelmed in obesity in adulthood is one explanation for this deposition. Acute energy restriction has been shown to reduce lipid deposits in the liver and reverse DM.
**Aims & Methods:** We aimed to investigate whether childhood weight status modifies the metabolic response following acute energy restriction in patients awaiting bariatric surgery. We analysed the self-reported childhood weight status recorded as a part of a randomised controlled trial (EnR-Lin study) comparing a food-based diet (FD) with a meal replacement plan (MRP) (LighterLife Ltd., U.K.) over two weeks prior to bariatric surgery. Clinical and anthropometric data and fasting blood were collected pre and post diet. Liver biopsies were taken during surgery.
**Results:** 60 participants were recruited and 54 completed the study; FD n = 26, MRP n = 28. Baseline demographic features (Table 1), dietary energy intake and weight loss post-diet were not significantly different between diet groups. However, the FD had higher reported intake of carbohydrate (median 52% compared to 38%), whereas the MRP had higher intakes of protein (median 37% compared to 30%) and fat (median 25% compared to 19%). All three macronutrient intakes were statistically different between groups ($P < 0.001$). 61% of all participants reported being overweight or obese as a child (OC) (n = 33). This subgroup had higher median body mass index (BMI) pre and post diet, pre 51.9kgm-2, post 50.3kgm-2, lean childhood BMI group pre 47.3kgm-2, post 46.2kgm-2. However, BMI change post-diet was not statistically significant between the two childhood weight groups ($P = 0.65$). Liver histology results post-diet were also not significantly different between diet groups. When separated for childhood weight status, as well as diet, OC on the FD had significantly higher levels of steatosis ($P = 0.006$), and portal inflammation ($P = 0.006$) compared to the lean group post-diet. There was no significant difference between results in childhood weight groups on the MRP. Reduction in insulin resistance as estimated by Homeostatic Model Assessment (HOMAIR) was significant following MRP, median (range) -1.0 (-26.3–5.9) ($p = 0.02$) when compared with FD -0.1 (-9.1–18.7) ($p = 0.91$). Reduction in HOMAIR remains significant only in the MRP OC group median (range) -1.0 (-26.3–3.0) $P = 0.01$ as opposed to lean -0.04 (-5.9–5.9) $P = 0.64$.

**Table 1:** Baseline characteristics of patients

| | Food-based diet (n = 26) | Meal plan (n = 28) |
|---|---|---|
| Gender: female/ male | 22/4 | 22/6 |
| Age in years: median (range) | 47 (25–65) | 42 (24–59) |
| Body mass index in kg/m$^2$: median (range) | 51.1 (42–69) | 50.1 (42–63) |
| No. with Type 2 Diabetes (%) | 8 (31) | 8 (29) |
| No. overweight or obese in childhood (%) | 17 (65) | 16 (57) |

**Conclusion:** People who were overweight or obese in childhood had a greater increase in insulin sensitivity following an energy restrictive meal replacement plan. This could indicate that both adipose tissue capacity and type of diet, including macronutrient intake, could affect insulin sensitivity following energy restriction in severe obesity.
**Disclosure of Interest:** E. Baldry: LighterLife provided their products free of charge for the study.
All other authors have declared no conflicts of interest.

## P1629 ARGON PLASMA COAGULATION FOR FAILED ROUX-AND-Y GASTRIC BYPASS (RYGB): AN ENDOSCOPIC ALTERNATIVE IN BARIATRIC PATIENTS WITH WEIGHT REGAIN

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**Introduction:** The weight regained has been a described growing problem in patients after bariatric surgery, especially at long term. This weight regained is multifactorial and often associated with dilation of gastrojejunostomy (GJ), allowing a faster gastric emptying and therefore greater food intake. For the patients with significant weight regain after failed conservative approach, some revisional procedures had be attempted and more recently endoscopic revisional procedures had being described.
**Aims & Methods:** To evaluate the safety and effectiveness of argon plasma coagulation (APC) decreasing the diameter of the gastro-enteric anastomosis in patients who have undergone Roux-and-Y Gastric Bypass (RYGB) for morbid obesity and regained weight associated to dilation of the GJ. From Jan-2014 to Feb-2016 385 RYGB subjects with weight regain, a dilated anastomosis (more than 18 mm in diameter) and at least 2 years from procedure were submitted APC application at GJ had their data reviewed from a prospective designed databank. Interval between an APC session applications was 60 days, with a maximum of 03 applications. APC set was at 2–3 L/m with 65–85 W. GJ diameter target was to reduced it up to 8–12 mm estimated with pre-measured open grasper. At first APC session pre-op weight and BMI, post-op weight nadir, actual weight and BMI and estimated diameter of GJ were the variables collected. At each following session weight, BMI and estimated GJ diameter were taken. Complications during treatment were also collected. Data were analyzed with descriptive statistics, student's t-test and Spearman correlation.
**Results:** Of the 385 patients, 85.2% were women and 14.8% were men. Average time between bariatric surgery and the first APC was 90.31 months (±43.32. Range: 24–182) and average weight regained in this interval was 23.36 kg (±11.72. Range: 5–64). The mean diameter of the anastomosis was 23.63 mm (±5.11. Range: 14–50) and the average number of APC sessions were 1.72 times (±0.68. Range: 1–3). The average reduction of anastomotic diameter was 14.71 mm (±7.21. Range: 2–35) and the final average diameter was 11.7 mm (±3.88. Range: 5–31). The average weight loss between the first and last APC was 14.08 kg (±6.21. Range: -3.42–34.77) and the average decrease of BMI was 4.79 kg/m$^2$ (±2.78. Range: -1.47–12.12). 93 patients (24.15%) did not achieve the target GJ diameter and 03 patient (0.78%) did not lose weight even with the desired GJ diameter. From the 88 subjects followed up to 6 months no regain weight was noted. Of the 385 patients APC, 42 (10.9%) required dilation balloon due to symptomatic stenosis at least once. No further complications were reported.
**Conclusion:** Argon Plasma Coagulation (APC) has been shown to be an effective and safe endoscopic technique for the reduction of gastro enteric anastomosis in patients undergoing bariatric surgery who have regained weight with dilation of the anastomosis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1630 ASSESSMENT OF THE EFFECTIVENESS OF DIET REDUCING WEIGHT GAIN IN POSTMENOPAUSAL OVERWEIGHT WOMEN

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**Introduction:** Obesity is a chronic metabolic disease associated with the pathological accumulation of body fat. During menopause a significant role in the biosynthesis of estrogen is caused by aromatase, including current in subcutaneous adipose tissue and adipocytes. It is responsible for the conversion of testosterone to estradiol and androstenedione to estrone. It contributes significantly to the increase in estrogen levels. Aromatase deficiency leads to impaired balance of estrogen-progesterone. As a result, excess fat is accumulated in the abdominal skin coatings, and visceral fat in the abdomen (android obesity "apple" type). This type of obesity is exposed more in women, who eat meals with to many calories and so low physical activity.
**Aims & Methods:** The aim of the study was to evaluate the effect of reducing diet in overweight and obese postmenopausal women on: concentration of selected sex hormones, feeling of hunger and satiety, psycho-emotional state. The study involved 97 women (44–65 aged) who consented to the study. The inclusion criteria were: lack of menstruation or irregular menstruation during last 12 months, right health condition, without coexisting organic diseases, normal body weight, obese, overweight woman, especially with gained weight during menopause, patients with vasomotor disturbances, hot flushes, headache, night sweats, patients with emotional disorders, fatigue, irritability, attention deficit disorder, memory and sleep impairment, mood swings, symptoms which testify dysthymia or depression. Patients were divided into three groups based on their BMI, which was calculated: group I control - 32 woman with normal body weight (BMI 18.5–24.9 kg/m$^2$), group II - 33 overweight woman (BMI 25–29.9 kg/m$^2$), group III – 32 obese woman (BMI > 30 kg/m$^2$). Each of the patients' body weight was measured. On this basis hiperalimentation syndrom was defined. Moreover waist / hip ratio (WHR - waist-hip ratio) was calculated. The content of fat was determined by measuring the skin-folds of fat and body composition analysis - using a body composition analyzer Bodystat QuadScan 4000, based on a non-invasive method of bioimpedance (BIA, bioelectrical impedance analysis). Immunoassay routinely determined in the serum concentration of the sex hormones estradiol, follicle-stimulating hormone (FSH), dehydroepiandrosterone sulfate (DHEA-S), and rostenedione. Patients completed nutrition questionnaires and in group II and III body weight reducing diet was recommended. Evaluation of the patients' mood was performed useing the Beck scale (BDI, Beck Depression Inventory). Evaluation of the patients' anxiety disorders was performed useing Hamilton Anxiety Scale (HAS, Hamilton Anxiety Scale) and intensity of appetite was determined using visual analogue scale – VAS. The study was performed at the beginning and after three months of observation.
**Results:** It was shown that diet reducing weight gain used for three months in postmenopausal women with a BMI above 25 kg/m$^2$ significantly lower BMI, reduces body fat and levels of sex hormones (DHEA-S, androstenedione and FSH – in obese women) and improves mood.
**Conclusion:** The use of a three-month diet reducing weight gain in postmenopausal women with overweight and obesity showed a signifficant affect on: reduction of body fat, mood improvement, development of healthy eating habits, improvement of emotional state, decrease in the levels of sex hormones (DHEA-S, androstenedione and FSH – in obese women) to the value similar for the group of women with normal body weight. In postmenopausal period overweight and obesity women should remain under the care of an experienced dietician. The well-constructed individual weight-reducing diet, systematic assessment of effectiveness and concious mind of its use can bring measurable benefits in the fight with obesity which is a modern disease of civilisation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1631 USING AN INTRAGASTRIC BALLOON FOR A SECOND TIME: IS IT A GOOD ATTEMPT?

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**Introduction:** The intragastric balloon use associated with a multidisciplinary approach aiming changes in lifestyle have shown efficacy in the treatment of overweight/ obesity and its corelated diseases. However, some patients may regain weight, and seek in the use of intragastric balloon for the second time a valid treatment option.
**Aims & Methods:** We aimed to evaluate the efficacy and complications of a second implant of intragastric balloon, with a minimum interval of six months between the removal of the first and second implant. Methods: We used intragastric balloons Orbera, with volume between 600–700 ml. The first balloon remained for a period of six months. The implant of the second balloon occurred after a minimum of six months in patients who had weight regained. Data were analysed using descriptive statistical methods and student t-test. Thet level of significance was set at $p < 0.05$.
**Results:** 71 patients had the balloon implanted for the second time at least six months (mean of 25.74 ± 12.94 months) after the removal of the first balloon. Of these, 25 had an early removal (balloon explant less than a month after

implantation) of the balloon due to intolerance (35.21%). Of the remaining 46 patients, 35 were women. The percent weight regain in relationship to first treatment weight lost was 99.71 ± 44.9 (range: 5.00–255.56). The patients showed a significant lower final BMI (mean: 29.61 ± 4.20 kg/m$^2$; range:20.08–42.98) than the initial BMI (mean: 35.27 ± 5.49 kg/m$^2$; range: 27.05–52.96) ($p < 0.0001$). The average weight loss in kilograms was 15.27 ± 8.78 (range 3.0–35.0). The percent total body weight loss (%TBWL) was 15.54 ± 7.95 (range: 3.26–40.23), and the percent excess weight loss (%EWL) of 60.57 ± 35.37 (range: 10.87–194.61). The success rate of treatment (> 25% EWL) was 91.30%. However, BMI reduction, weight loss in Kg, %TBWL and %EWL were significantly lower than in the first treatment ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$, $p = 0.0004$, respectively)

**Conclusion:** Use an intragastric balloon for the second time to treat obesity still proves to be effective, though to a lesser extent than in the first treatment, and with a high rate of complications (early balloon removal), a fact that should be thoroughly discussed and considered with the patient before making the choice of using this treatment again.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1632 CD24 POLYMORPHISMS ARE ASSOCIATED WITH OBESITY RISK

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**Introduction:** Obesity is a global epidemic and a major risk factor for various health catastrophes. It is amultifactorial disease and has genetic and environmental etiology. Several studies have suggested candidate genesthat may predispose to obesity. CD24 is a small, mucin-like glycoprotein that is expressed in many humanmalignancies (Sagiv, et al., 2006). We have recently found that CD24 knockout male (but not female) mice are obesewith hyper insulin sensitivity than their wild-type (WT) littermates. Four single nucleotide polymorphisms (SNPs) in theCD24 gene are known to affect cancer risk and autoimmune diseases. C170T CD24 SNP results in the replacementof alanine by valine. This amino acid change is associated with increased risk for multiple sclerosis (MS), systemiclupus erythematosus (SLE) and cancer risk (Huang, et al., 2015).

**Aims & Methods:** We aimed to evaluate whether SNPs in the CD24 gene are associated with increased obesity risk. Methods: Genomic DNA was extracted from peripheral blood leukocytes of 158 obese Israeli patients (BMI ≥ 30; 122males and 36 females), as well as age and gender-matched healthy controls (BMI ≤ 27; 178 males, 23 females).Samples were genotyped for the CD24 SNPs: C170T (rs8734), TG1527del (rs3838646), A1626G (rs1058881) andA1056G (rs1058818) by real-time PCR using Custom TaqMan® SNP allelic discrimination assays. $\chi 2$ test was usedto examine whether the CD24 gene polymorphism is associated with obesity. An association was consideredstatistically significant if $p < 0.05$.

**Results:** C170T SNP is more prevalent in obese male than in normal weight males ($p = 0.087$), even after ageadjustment ($p = 0.028$; correlation coefficient = 1.367). This trend was not observed in obese females. This correlationbecomes more significant for the obese males (>50 year) (p=0.03; correlation coefficient = 3.558), Nocorrelation was found between the other three SNPs, in the 3'UTR, and the risk for obesity.

**Conclusion:** The genetic variation C170T CD24 may be an important determinant for obesity in men, in particularabove 50 year old. There is a need for a prospective life style intervention, in this group of patients, which may preventobesity later in life.

**Disclosure of Interest:** N. Arber: Consultation Fee: Bio-View, Check-Cap, Bayer Stock Shareholder: Micromedic, GI-View
All other authors have declared no conflicts of interest.

## P1633 LYSOZYME FRACTION FROM DONKEY MILK (DM) SUPPORTS VISCERAL ANTINOCICEPTIVE PROPERTIES OF DM, REDUCES PROTEASE ACTIVITY AND RESTORES ANTIMICROBIAL LEVELS IN PANETH CELLS IN A MODEL OF CHRONIC STRESS IN MICE

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**Introduction:** Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain or discomfort associated with a low-grade mucosal inflammation and luminal protease activity increased [1]. Stressful life events trigger IBS symptoms. Chronic stress paradigms were developed in animals to mimic changes in visceral sensitivity seen in IBS patients. In mice, passive avoidance stress is associated with hypersensitivity to rectal distension. Several studies suggest that probiotics or specific dietary interventions may have beneficial effects in IBS patients [2]. Donkey milk (DM) has important nutritional properties for humans linked to its similar composition to human milk. In particular, DM presents high levels of antimicrobial peptides such as lysozyme and lactoferrin [3].

**Aims & Methods:** Therefore, using a chronic water avoidance stress (WAS) model, we aimed to evaluate whether 1) WAS modified visceral sensitivity, serine protease activity in feces, and lysozyme expression in Paneth cells (PC) and 2) an oral DM supplementary diet can alleviate these alterations and 3) the positive effects of DM are supported by the abundance of antimicrobial peptides in DM i.e. lysozyme. Male C57BL/6 mice were used in this study. During 9 days, mice were submitted to a sham stress or to a WAS session for 1 h and orally received DM (0.2 mL, 5400UI of lysozyme), fraction of DM containing lysozyme (FL) (equivalent dose of lysozyme) or water (0.2 mL). In a 1$^{st}$ series of experiments, at day 9, visceral sensitivity response to CRD was assessed after the last WAS or sham session. In a 2$^{nd}$ series of experiments, both feces and ileal samples were collected to quantify fecal serine protease activity by enzymatic assay, and the lysozyme expression in PC by immunostaining, respectively.

**Results:** Compared to sham treatment, WAS significantly induced visceral hypersensitivity in response to CRD, significantly increased fecal serine protease activity, and promoted a drastic decrease of lysozyme levels contained in ileal PC. Under basal conditions a treatment with DM or FL did not modify visceral sensitivity in response to CRD. A chronic administration of DM or FL was able to significantly reduce abdominal contractions induced by WAS. In addition, DM and FL normalize both the fecal serine protease activity and lysozyme levels in PC altered by WAS.

**Conclusion:** DM given as a supplementary diet alleviates WAS-induced functional alterations i.e visceral hypersensitivity, fecal serine protease increased and the fall in antimicrobial peptides contained in PC. Interestingly, all these beneficial effects are supported by the high level in Lysozyme contained in DM.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1635 DEVELOPMENT AND VALIDATION OF A GLIADIN 33-MER-BASED IMMO-ASSAY FOR THE MONITORING OF A GLUTEN-FREE DIET

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**Introduction:** Even today, strict adherence to a gluten-free diet is regarded as the only effective therapy for coeliac disease. However, suitable markers for the monitoring of diet adherence and detection of gluten contaminants are still lacking. The commonly tested IgA and IgG antibodies are of limited use, since their decline under a gluten-free diet is protracted (up to 1 year).

**Aims & Methods:** Given the high stability of various 3-mer gliadin peptides (33mPs), a sandwich ELISA was developed based on monoclonal antibodies. After extraction of ethanol, this ELISA allows the definition of related peptides up to 2 ng/g stool and shows a linear correlation two times the power of ten.

**Results:** In subjects (n = 5) with a daily intake of 20 g gluten, the test showed 117.8 (68.6–234.1)ng 33mPs/g, compared to 1.8 (0.4–3.0)ng 33mPs/g in individuals adhering to a gluten-free diet.

**Conclusion:** In this cohort, levels of 3-mer-rich gluten peptides in stool showed a significant positive correlation to respective daily gluten intake. The novel ELISA is the first test to allow realtime monitoring of adherence to a gluten-free diet and detect possible gluten contaminants.

**Disclosure of Interest:** D. Rehan: Dmitri Rehan is an employee of Immundiagnostik AG, Bensheim, Germany.
F. Armbruster: Franz-Paul Armbruster is managing director of Immundiagnostik AG, Bensheim, Germany
J. Stein: Jürgen Stein has received fees for consultancy and lectures from Immundiagnostik AG, Bensheim, Germany

## P1636 ANALYSIS OF TREATMENT RESULTS WITH TEDUGLUTIDE ON INTESTINAL ABSORPTION AND NUTRITIONAL STATUS IN PATIENTS WITH SHORT BOWEL SYNDROME

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**Introduction:** Glucagon like Peptide-2 (GLP-2) is a protrophic gastrointestinal hormone that promotes regeneration of the intestinal mucosa and improves

intestinal absorptive function. Teduglutide (TED), a GLP-2 analogue, was recently approved for the treatment of short bowl syndrome (SBS) in patients with chronic intestinal failure who are dependent on parenteral nutrition (PN).
**Aims & Methods:** Single center-based clinical and paraclinical data from patient records of 11 patients with benign SBS were retrospectively analysed. Nutritional status was assessed by body weight, albumin and transferrin concentration and bioelectrical impedance analysis (BIA).
**Results:** Fifteen patients have been treated with TED at this center thus far. This is an interim analysis of 11 patients. Twelve weeks after initiation of TED treatment (0.05 mg/kg) patients had a 28% reduction in PN volume needs ($n = 10$; $p = 0.007$) and a 15% reduction in kcal needs ($n = 10$; $p = 0.027$) with a simultaneous weight increase of 4.5% ($n = 8$; $p = 0.04$). After a mean treatment of 43 weeks (SD = 20.1 wks.) patients gained a mean of 1.1 total infusion-free days and two (18%) out of 11 patients were completely weaned off PN. Albumin und transferrin levels remained constant throughout PN-reduction. Patients had a significant reduction in stool frequency and an increase in stool consistency ($n = 10$; $p = 0.003$ and $p = 0.03$ resp.). Analysis of BIA parameters showed a significant increase in intracellular water ($n = 5$; $p = 0.041$), lean body mass and body fat percentage ($n = 5$; $p = 0.043$) demonstrating a specific beneficial effect on body composition.
**Conclusion:** The analysis of initial clinical data on long-term use of TED for SBS patients demonstrates improved intestinal function through increased fluid and nutrient absorption as well as increased body weight. Furthermore functionally relevant body composition was improved as shown by BIA-analysis of nutritional status beyond body weight. Study of TED effects in clinical routine will support future decision making in clinical practice.
**Disclosure of Interest:** U. Pape: Speaker Bureau of Shire Pharmaceuticals
All other authors have declared no conflicts of interest.

## P1637 FOLATE SUPPLEMENTATION PROMOTES STEMNESS ON HT-29 COLORECTAL CANCER CELL LINE VIA NOTCH1 SIGNALING PATHWAY

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**Introduction:** Folic acid (FA) consumption at high levels has been associated with colon cancer risk. Several mechanisms have been proposed to explain this association. The Notch signal pathway has been implicated in the regulation of cellular proliferation.
**Aims & Methods:** Folic acid promotes **stemness** on HT-29 cell line, via Notch1 signaling activation. Methods: We cultured HT-29 cells with 3 different conditions, without folic acid, with 400 nM folic acid or 5-methyl tetrahydrofolic acid (5-MTHF). We analyzed the expression of stem cell markers and Notch-1 pathway related genes by real time PCR in all 3 conditions.
**Results:** The supplementation with folic acid or 5-MTHF increase migration of HT-29 cells, the expression of NANOG, SOX-2, POUF-5 (stem cell markers, $p < 0.05$) and HES-1 (activation of Notch-1 pathway, $p < 0.05$).
**Conclusion:** Folic acid or 5-MTHF supplementation increase **stemness** and migration on HT-29 cell line that could be associated with aggressiveness of colorectal cancer.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1638 ORAL INTAKE OF PURIFIED AQUEOUS SOLUTION OF OAT BETA-GLUCANS HAS LIMITED EFFECT ON OXIDATIVE STRESS IN PATIENTS WITH CHRONIC GASTRITIS: A PILOT PHASE II CLINICAL TRIAL

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**Introduction:** Numerous clinical studies have demonstrated that consumption of oat beta-glucans has been associated with potential health benefits for humans, such as reduction of postprandial glucose, decreasing serum cholesterol or colorectal cancer prevention. Many studies also have shown that these natural polysaccharides have antioxidant properties. To our knowledge, no prior study has been conducted to determine the antioxidant effects of oat beta-glucans supplementation in chronic gastritis patients.
**Aims & Methods:** The aim of this study was to determine the effect of high (2 000 000 – 3 000 000 g/mol) or low (30 000 – 90 000 g/mol) molecular weight of oat beta-glucans on selected parameters of the antioxidant potential of the blood and plasma samples in patients with chronic gastritis. 48 patients aged 23–74 years were randomly assigned to either a placebo group, receiving an oral dose of 100 ml 3% solution of potato starch (Placebo), or to one of the treatment groups receiving oral dose of 100 ml high (G1) or low (G2) molecular weight beta-glucans for 4 weeks. Easily digestible diet was recommended for all groups. Plasma total antioxidant status (TAS) and the levels of glutathione peroxidase (GPx), glutathione reductase (GR) and whole blood superoxide dismutases (SODs) were examined using Randox Reagents (United Kingdom). Whole blood reduced (GSH) and oxidized (GSSG) glutathione level were measured according to Rebrin, Forster, and Sohal (2007).
**Results:** Before the intervention, activity of SODs and GR was significantly higher in G2 group compared with placebo group. The results showed that the activity of GR was significantly lower after the dietary supplementation of G2. The level of SODs observed in the placebo group was significantly higher than those observed in other grups. The diet supplementation of G1 significantly increased levels of GSSG in the blood. GSSG levels also increased in Placebo. In the case of GPx activity we observed a statistically significant decrease in placebo group. No significant changes were observed regarding other parameters examined.
**Conclusion:** Changes limited to oxidized glutathione and glutathione reductase levels show that selected dose and form of oral beta-glucans exert no significant effect on oxidative stress in patients with chronic gastritis.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1639 CT-GUIDED PERCUTANEOUS GASTROSTOMY/ JEJUNOSTOMY FOR FEEDING AND DECOMPRESSION

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**Introduction:** A very effective method for long-term enteral feeding or stomach decompression is the use of a percutaneous gastrostomy (PEG) or sometimes jejunostomy (PEJ). Under certain circumstances, such as inadequate transillumination, endoscopic placement of PEG/PEJ-tubes is impossible. In these cases computed tomography (CT)-guided PEG/PEJ may represent an alternative technique. In this study, we evaluate indications, results and complications of CT-guided PEG/PEJ.
**Aims & Methods:** A total of 102 consecutive referred patients were enrolled in the study. Patients came to the endoscopy unit of our department to undergo a CT-guided PEG/PEJ for long-term intragastric/intrajejunal feeding ($n = 57$) or decompression ($n = 45$). The majority of the patients ($n = 98$) received a pull-through PEG/PEJ with simultaneous gastroscopy/jejunoscopy. Dose length product (DLP) and the effective dose (in mSv) for every patient was calculated.
**Results:** Altogether, gastrostomy/jejunostomy tube placement was successful in 87.3% of patients (89/102). Feeding PEG/PEJ-tube placement was successfully completed in 91.2% of patients (52/57), decompressive PEG/PEJ-tube placement was likewise successfully completed in 82.2% of patients (37/45). No procedure-related mortality was observed. Minor complications such as tube dysfunction, local bleeding, minimal leakage or local skin infection were observed in 13 patients. Complication rate was similar in both the feeding and the decompression group ($p = 0.9$).
**Conclusion:** CT-guided PEG/PEJ is a feasible and safe method with a low procedure-related morbidity rate for the group of patients where endoscopic placement via transillumination is not successful. Thus, the procedure is an attractive alternative to surgical tube placement. Long-term complications, which are mainly tube disturbances, can be treated easily.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1640 PERFORMANCE OF THREE PROGNOSTIC RISK SCORES IN PREDICTING OUTCOMES IN ELDERLY NON-MALIGNANT PATIENTS AFTER PERCUTANEOUS GASTROSTOMY

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**Introduction:** Percutaneous endoscopic gastrostomy (PEG) is a safe and useful method for patients who have difficulty in oral feeding with normal functioning gastrointestinal (GI) tract. Percutaneous endoscopic gastrostomy is mainly indicated for patients who are expected to require non-oral nutritional support for more than 4 weeks.

**Aims & Methods:** The aims of this study were to determine the performance of "Geriatric Nutritional Risk Index" (GNRI), "Malnutrition Universal Screening Tool" (MUST) and "Portsmouth-Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity" (P-POSSUM) for predicting short and long-term mortality in elderly patients who had undergone PEG procedure due to non-malignant conditions. This study included 155 elderly patients patients who had undergone percutaneous endoscopic gastrostomy procedure due to non-malignant conditions. GNRI, MUST and P-POSSUM scores were calculated. The ability of these scores to predict short and long-term mortality was determined.
**Results:** The overall mean survival period was $9.59 \pm 6.0$ months and mortality rate was 80.6%. The performance of GNRI was superior to MUST and P-POSSUM in predicting long-term survival of PEG patients; 94.1% of patients were alive with a cut-off value of 90 for GNRI (sensitivity: 92% CI 85.9–95.6 and specificity: 90% CI 74.3–96.5). Kaplan-Meier survival analysis of GNRI showed that patients ($n = 7$) with a GNRI score of $> 98$ before the PEG procedure had the longest survival time, while patients ($n = 102$) with a GNRI score of $< 82$ had the worst outcome.
**Conclusion:** A scoring system such as GNRI should be considered as a risk scoring system for predicting early and late mortality at percutaneous endoscopic gastrostomy and also assist in making decisions such as timing of percutaneous endoscopic gastrostomy procedure.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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### P1641 KNOWLEDGE, ATTITUDES AND EXPERIENCES OF INTERNAL MEDICINE TRAINEES TOWARDS ENTERAL FEEDING TUBE: RESULTS FROM MULTICENTER SURVEY OF CURRENT PRACTICE


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**Introduction:** Although use of enteral tube feeding is a common condition in patients who compromise the passage of food along the digestive tract, there is limited data available on how well internal medicine trainees know about enteral feeding tube. This study aimed to identify current knowledge, attitudes and experiences of internal medicine trainees towards enteral feeding tube in Korea.
**Aims & Methods:** A prospective survey was performed among trainees of internal medicine in 13 hospitals. A 17-item questionnaire addressed knowledge about enteral feeding tube, experience of complications and their clinical practice changes to these complications.
**Results:** Overall, 269 internal medicine trainees (162 male, mean age $31.54 \pm 3.30$) completed the questionnaire. Over half of the respondents (150, 56%) answered that they often encounter patients who use enteral feeding tube. However, only 39.2% of respondents had ever received education about enteral feeding tubes. Only 38.8% of trainees felt they had an adequate knowledge about this subject and 29.1% stated that they provided appropriate information to patients with enteral nutrition (EN). The majority agreed to the cost effectiveness and priority of EN compared to peripheral nutrition. However, only 31.3% correctly estimated the optimal replacement time of nasogastric (NG) tube. Although over half of the respondents had experiences complications of NG tube, their attitude toward these complications varied widely. In addition, 86.9% of trainees answered that they were willing to receive education regarding enteral feeding tube, if provided.
**Conclusion:** Many internal medicine trainees lack knowledge about enteral feeding tubes and their practice varied widely. Implementation of an adequate training system with regard to enteral feeding tube is necessary for internal medicine trainees to improve the quality of healthcare.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1642 THIRTY-DAY MORTALITY AFTER PERCUTANEOUS GASTROSTOMY BY ENDOSCOPIC VERSUS RADIOLOGIC PLACEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS


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**Introduction:** A percutaneous gastrostomy can be placed either endoscopically (percutaneous endoscopic gastrostomy, PEG) or radiologically (radiologically inserted gastrostomy, RIG). However, there is no consistent evidence of the safety and efficacy of PEG compared to RIG. Recently, 30-day mortality has become considered as the most important surrogate index for evaluating the safety and efficacy of percutaneous gastrostomy.
**Aims & Methods:** The aim of this meta-analysis was to compare the 30-day mortality rates between PEG and RIG. Major electronic databases (MEDLINE, EMBASE, Scopus, and Cochrane library) were queried for comparative studies on the two insertion techniques of gastrostomy among adults with swallowing disturbance. The primary outcome was the 30-day mortality rate after gastrostomy insertion. Forest and funnel plots were generated for outcomes using STATA version 14.0.
**Results:** Fifteen studies ($n = 2.183$) met the inclusion criteria. PEG was associated with a lower risk of 30-day mortality after tube placement compared with RIG (odds ratio [OR] 0.60; 95% confidence interval [CI] 0.38–0.94; $P = 0.026$). The pooled prevalence of 30-day mortality of PEG was 5.5% (95% CI, 4.0–6.9%) and that of RIG was 10.5% (95% CI, 6.8–14.3%). No publication bias was noted.
**Conclusion:** The present meta-analysis demonstrated that PEG is associated with a lower probability of 30-day mortality compared to RIG, suggesting that PEG should be considered as the first choice for long-term enteral tube feeding. Further prospective randomized studies are needed to evaluate and compare the safety of these two different methods of gastrostomy.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

### P1643 SERUM TRACE ELEMENTS AND PROTEINS BEFORE ENDOSCOPIC GASTROSTOMY AND DURING LONG-TERM ENTERAL FEEDING


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**Introduction:** Patients who underwent endoscopic gastrostomy (PEG) present protein-energy malnutrition, but little is known about Trace Elements (TE), Zinc (Zn), Copper (Cu), Selenium (Se), Iron (Fe), Chromium (Cr).
**Aims & Methods:** Our aim was to evaluate serum protein and TE evolution during the first 3 months after gastrostomy with homemade PEG feeding, and the relationship of TE with proteins and the nature of the underlying disorder. Methods: Prospective observational study during a 3-month period after gastrostomy. Data was collected at initial PEG procedure (T0), after 4 (T1) and 12 weeks (T3). Initial evaluation included: age, gender, underlying disorder causing dysphagia (Neurological Dysphagia: ND; Head and Neck Cancer: HNC), NRS-2002, BMI. At T0, T1 and T3 a blood sample was collected for TE, albumin and transferrin. We used ferrozine colorimetric method for Fe evaluation; Inductively Coupled Plasma-Atomic Emission Spectroscopy for Zn/Cu; Furnace Atomic Absorption Spectroscopy for Se/Cr. After the gastrostomy all patients were fed with homemade meals.
**Results:** Initial: 146 patients (89 males), 21–95 years: HNC-56; ND-90. Low BMI in 78. NRS-2002 $\leq$ in all patients. At T0 low values mostly for Zn ($n = 122$) and Fe ($n = 69$), but less for Se ($n = 31$), Cu ($n = 16$), Cr ($n = 7$); low albumin in 77, low transferrin in 94 and 66 with both proteins low. Only for Zn, significant differences ($t_{140.326} = -2.642$, $p < 0.01$) between the groups of underlying disease (low in 93% of HNC patients, 78% ND patients). Except for Zn, low TE cannot be related with age, gender, BMI, serum proteins levels or underlying disease. There was a correlation between albumin and Zn ($r = 0.197$, $p = 0.025$), and Fe ($r = 0.415$, $p = 0.000$). Evolution T0-T3: Serum protein increase, most patients reaching normal, with significant differences between the three moments for albumin ($p = 0.000$) and transferrin ($p = 0.014$). For TE we observed slow evolution. Most patients still displaying low Zn at T3, with significant differences between the 3 moments ($p = 0.011$). Other TE increased, but normalization was incomplete at T3. For Fe positive correlations were detected with albumin and transferrin. No relationship was found at T1 and T3 between Se, Cu and Cr with the groups of underlying diseases or proteins.
**Conclusion:** When gastrostomy was performed, patients display low serum proteins and TE namely Zn, but also Fe, less striking regarding others TE. Low proteins were associated with low TE. Low serum proteins are normalized but low TE cannot be correct during 3 months of homemade enteral feeding. Teams taking care of PEG patients should use systematic TE supplementation.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1644 TREATMENT OF SHORT BOWEL SYNDROME WITH GLP-2-ANALOGUE TEDUGLUTIDE – FIRST CLINICAL DATA FROM TUEBINGEN UNIVERSITY HOSPITAL, GERMANY

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**Introduction:** Teduglutide is a novel therapeutic agent in the therapy of short bowel syndrome. In phase III - trials it proved to significantly reduce parenteral nutrition. Since its introduction in 2014 we have treated 15 patients in our outpatient centre.
**Aims & Methods:** Data was aquired with the help of a specialized nursing service. Thirst, body weight, oral fluid intake, urinary output, frequency of bowel movements and bowel movement consistency as well as amount of parenteral nutrition (days per week as well as total intake) were regularly measured. The reduction of parenteral nutrition was decided upon individually with regard to clinical parameters.
**Results:** We collected data from 11 of our 15 patients. All patients wished to continue therapy with Teduglutide and declared a general improvement of their situation. The average lenth of treatment (in march 2016) was 26.4 weeks (7.0–56.0, SD 16.1. All five patients with inial heavy thirst lost it within the first four weeks of treatment. In four patients days of parenteral nutrition was reduced by one day per week. After 12 weeks ($n = 8$, $\mu = 13.1$, $SD = 6.7$, $p < 0.05$) and 24 weeks ($n = 7$, $\mu = 14.4$, $SD = 8.7$, $p < 0.05$) there was a significant reduction in bowel movement frequency (baseline $\mu = 18.0$, $SD = 7.0$). All patients declared a solidification of their bowel movements. Body weight, urinary output and days of parental infusion per week did not change significantly.
**Conclusion:** All patients tolerated Teduglutide well and wished to continue treatment. Reduction of thirst (which was 100% if present before treatment) as well as significant reduction in bowel movement frequency seem to be early clinical markers for a response to treatment. Other markers of bowel functioning as body weight, urinary output and demand in parenteral nutrition vary strongly within the different individuals and demanda longer observation period. Reduction of parenteral nutrition takes time and should not be hastened. Independently from parenteral nutrition patients report a considerable improvement of their situation under treatment with Teduglutide.
**Disclosure of Interest:** J. Wehkamp: receives research funding from Shire Pharmaceuticals
All other authors have declared no conflicts of interest.

## P1645 ADJUSTING THE TIMING OF REFEEDING AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT - WHEN EARLY IS NOT TOO EARLY!

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**Introduction:** Although historically the timing of refeeding after the placement of a percutaneous endoscopic gastrostomy (PEG) was delayed over a period of 24 hours, several studies have shown that shortening of this interval is safe.
**Aims & Methods:** The aim of this study was to compare the safety of refeeding at 4 hours with refeeding at 24 hours after PEG placement in a center with a specialized multidisciplinary consultation. This was a prospective single-center, randomized, controlled study, including 81 patients who were submitted to PEG between May/2014 and February/2016. Two groups were established: group A (refeeding 4 hours after PEG placement) included 33 patients, while group B (refeeding 24 hours after PEG placement) included 48 patients. For comparison of complications between the two groups $\chi^2$, t -student and Fisher's exact tests were used.
**Results:** From the 81 enrolled patients enrolled, 60 were women and the average age was $79 \pm 11$ years. The main indications for PEG placement were dysphagia after ischemic stroke (33.3%), Alzheimer's disease (25.9%), and vascular dementia (18.5%). Regarding the complications registered after the procedure, there were no significant differences between the groups, namely on inflammation of the stoma ($p = 1.000$), gastric contents leakage ($p = 0.133$), fever ($p = 0.475$), vomiting ($p = 0.153$), or local bleeding ($p = 0.133$). Although gastric residual volume was greater in group A, this difference was not statistically significant (47 vs. 20 mL; $p = 0.183$). Melena, diarrhea or peritonitis were not reported in any of the patients during the post-procedural period. During the follow-up, 6 patients died, but none of the deaths were related to PEG placement, and there were no significant differences between groups ($p = 1.000$).
**Conclusion:** Refeeding patients as early as 4 hours after PEG placement was not associated with an increased number of local or systemic complications, thus it should be routinely implemented in all patients.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## P1646 ANAESTHETIST ASSISTED PERCUTANEOUS ENDOSCOPIC GASTROSTOMY WITH GASTROPEXY; A SAFE AND EFFICIENT PROCEDURE

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**Introduction:** Percutaneous endoscopic gastrostomy (PEG) with gastropexy is recommended for percutaneous feeding tube placement in patients with oropharyngeal or oesophageal malignancy. It is also advantageous in patients with neuromuscular disease as it allows the placement of a balloon device saving them from the need of a second intervention. The aim of this study is to to evaluate the efficacy and safety of PEG gastropexy performed with an anaesthetist's assistance. The study was particularly concerned with comfort scores, morbidity and mortality.
**Aims & Methods:** Adult PEG gastropexies performed electively at a district general hospital between June 2011 to June 2015 were evaluated retrospectively. All the procedures were performed by two experienced endoscopists with an anaesthetist's assistance. Midazolam and remifentanil via target controlled infusion (TCI) were used for deep analgesia. Age, gender, physical status according to the American Society of Anaesthetists (ASA) classification system, indication for procedure and comfort scores using the modified Gloucester Scale (1 = no discomfort to 5 = severe discomfort) were recorded. Immediate complication, 8-day readmission and 30-day mortality rate were also measured.
**Results:** A total of 165 patients underwent 166 procedures. The mean age was 63+/- 9.06 years and the male to female ratio was 3:1. 143 patients were classified ASA II, 21 ASA III and 1 ASA IV. Indications included oropharynageal malignancy (152), motor neuron disease (7), oesophageal malignancy (3), thyroid malignancy (2), achalasia (1) and chronic liver disease (1). All procedures were successfully completed. There were no immediate complications. The mean comfort score was 1.11 ($SD = 0.37$). The mean hospital stay was 1.3 days ($SD = 2.18$) days. The mortality rate 30 days post procedure was 0%. 4 patients were readmitted within 8 days post procedure. 2 of these admissions were related to the procedure. One was due to a dislodged PEG tube and the other due to infection around the PEG site.
**Conclusion:** Anaesthetist-assisted PEG gastropexy is a safe and efficient procedure. This service can be implemented in a district general hospital requiring short hospital stay even for patients at risk of ventilatory impairment.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## P1647 EFFECT OF ENTERAL NUTRITION ON METABOLIC SYMDROME WITH NONALCOHOLIC FATTY LIVER DISEASE IN ELDERLY PATIENTS

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**Introduction:** We aimed to observe the effects of enteral nutrition on metabolic symdrome (MS) with nonalcoholic fatty liver disease (NAFLD) in elderly patients.
**Methods:** The 109 patients with MS and NAFLD were randomized into group EN ($n = 55$) and TPN ($n = 54$). The EN group received aggressive enteral nutrition therapy; the TPN group got the treatment of total parenteral nutrition. The body mass index (BMI), the blood liver function, glucose, blood liquid and hepatic ultrasonography were observed in two groups.
**Results:** After treatment of 1 month, there was significant improvement in the level of BMI, 2HBG, HbA1c, ALT, AST, BIL, TG, LDL-C ($P < 0.05$) in two groups in comparison with pretherapy. In the changes, of hepatic ultrasonography was improved but not significantly. In the TPN group the observations were counter to the EN group.
**Conclusion:** EN support is superior to TPN in aspects of avoiding increasing the glucose and fat metabolism, in imaging changes of NAFLD, and could improve treatment in elderly patients with MS and NAFLD.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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WEDNESDAY, OCTOBER 19, 2016 10:30–12:00
VIDEO CASE SESSION – ROOM E1

## VC01 A CASE OF ESOPHAGEAL CANCER DERIVED FROM GIANT DIVERTICULUM TREATED BY ESD AND THORACOSCOPIC COLLABORATION SURGERY

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**Introduction:** Endoscopic submucosal dissection (ESD) has been widely accepted for treatment of early gastrointestinal cancer in Japan. The main complication of ESD is perforation. ESD for esophageal squamous cell carcinoma (SCC) existing in a diverticulum is impossible to perform without perforation. Therefore, we performed a combination therapy between ESD and thoracoscopic surgery for the lesion.
**Aims & Methods:** A 60-year-old male who had esophageal SCC was referred to our hospital. Esophagography showed a diverticulum in the right side of middle thoracic esophagus. Endoscopy revealed a reddish 0-IIc lesion within the diverticulum and the lesion spread around the diverticulum. NBI endoscopy showed a well-demarcated brownish area. And, a loop-like irregular micro-vascular pattern was observed by NBI magnified endoscopy. A well-demarcated unstained area was revealed by iodine staining, and the size was more than half circumference. No lymph node and distant metastasis was diagnosed by CT scan and EUS. Therefore, the SCC was diagnosed as T1a without lymph node metastasis. The standard therapy for esophageal SCC in diverticulum is esophagectomy, because ESD may cause perforation. But, the patient didn't want to be treated by esophagectomy. Therefore, a corroboration therapy between ESD and thoracoscopic surgery was planned.
**Results:** At first, esophageal diverticulum was observed by a surgeon with thoracoscopy after intubated general anesthesia, and adhesion around the diverticulum was dissected. Next, ESD was performed by a hook knife. Severe fibrosis existed around the diverticulum, therefore proper muscle was cut with the diverticulum resulting a big perforation. Lung was observed through the perforation after ESD. Finally, the perforation was closed by the surgeon using thoracoscopy. 50 mg triamcinolone was injected into the submucosal layer on the artificial ulcer to prevent stricture. The patient felt no complaint, and was discharged 7 days after this treatment. The size of resected specimen was 47 x 43 mm, and pathological diagnosis was squamous cell carcinoma in esophageal diverticulum, the invasion depth was T1a; however SCC invaded submucosal layer through proper esophageal gland in only one point without lymph vascular involvement, lateral and vertical margin was negative, the size of SCC was 36 x 25 mm. R0 resection was achieved by this combination therapy.
**Conclusion:** Combined therapy of ESD and thoracoscopy is a minimally invasive surgery. Therefore, it is a good option for the treatment of a superficial SCC with esophageal diverticulum.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## VC02 NOVEL TECHNIQUE TO RELAX THE LOWER ESOPHAGEAL SPHINCTER (LES) DURING CHALLENGING PER ORAL ENDOSCOPIC MYOTOMY (POEM)

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**Introduction:** Amyl nitrite is easily administered in an inhaled form and results in potent, short-acting (2 minutes) smooth muscle relaxation. Therefore, amyl nitrite can be used to transiently relax the lower esophageal sphincter (LES). Its use has been reported during barium esophagogram in order to distinguish patients with pseudoachalasia from those with idiopathic achalasia. One study demonstrated that diameter of the LES increased by more than 3 mm in patients with idiopathic achalasia in response to amyl nitrite.[1] Peroral endoscopic myotomy (POEM) is a purely endoscopic procedure aimed at obliterating pressure at the LES for the palliation of symptoms in achalasia. POEM involves creation of a submucosal tunnel for which dissection of submucosal fibers should be carried out close to the muscle layer surface to avoid mucosal injury. Intraprocedurally, when the LES is tight the dissection of the fibers can be challenging to perform safely without a risk of mucosal injury.
**Aims & Methods:** In this video we demonstrate two cases of utilizing amyl nitrite inhalation to relax the lower esophageal sphincter to facilitate submucosal tunneling during POEM.
**Results:** Cases: The first case is a 59-year-old male who underwent POEM for type III achalasia. During submucosal tunneling, the distal esophagus and LES were spastic inhibiting the advancement of the endoscope through the LES. The decision was made to use amyl nitrite was used to relax the LES. A 10 cc syringe was connected to the ventilation circuit. One ampule of amyl nitrite was placed inside the syringe. Patient was ventilated with a bag for 10 minutes. A second ampule of amyl nitrite was added and the distal esophagus and LES effectively relaxed and facilitating creation of the submucosal tunnel. During amyl nitrite administration his heart rate maximally increased by 10 bpm from base line of 70 bpm and blood pressure decrease to 95/68 from base of 117/70 mmHg. The second case is a 38-year-old female who underwent POEM for type II achalasia. During POEM, the LES found to be tight preventing effective and safe submucoal tunneling. A total of 9 ampules of amyl nitrite were given to relax the LES and facilitate submucosal dissection and tunneling safely. Her heart rate transiently increased by a maximum of 10 bpm from baseline to a max 95 bpm and the blood pressure drop to 80 mmHg from a baseline of116 mmH. Both patients were admitted to the hospital for observation as part of routine clinical care. Cine eophagogram 24 hours later showed no leak. Both patients were discharged home on soft diet and returned to clinic 4 weeks later with complete resolution of the symptoms.
**Conclusion:** Conclusion: Amyl nitrite is safe and effective method to relax the LES (figure 1). This technique may be utilized in patients where the creation of a submucosal tunnel through the LES may have otherwise not been safely performed.
**Disclosure of Interest:** M. Khashab: Dr. Khashab is a consultant for Boston Scientific. All other authors have no relevant disclosures.
All other authors have declared no conflicts of interest.

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## VC03 NOVEL METHOD TO AVOID THE MIGRATION OF THE METALLIC STENT INTO THE OMENTAL BURSA DURING EUS-GUIDED HEPATOGASTROSTOMY

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**Introduction:** Hepatogastrostomy (HGS) is a novel method of the biliary decompression performed under the EUS. The migration of the metallic stent (MS) into the omental bursa is an ominous complication. The MS migration is caused by an inward pushing force of the gastric wall induced by the released side of the MS during the deployment, because the spindle shape of the released side of the MS makes a pushing force from outside due to the dynamic reason. To avoid the migration, MS is released after the echoendoscope is drawn back at the level of lower esophagus, when the introducer is inserted into the intrahepatic bile duct. However, under this method we cannot verify the MS release visually.
**Aims & Methods:** To achieve the successful deployment under visual condition, we conduct the pilot study of the intra-conduit release of the metallic stent before the deployment. The safety and feasibility are validated. HGS was performed with liner array echoendoscope and 19 G needle. After puncturing an intrahepatic duct, 0.025 inch guidewire (Visiglide, Olympus, Japan) was inserted. Then, the double lumen catheter (Uneven Double Lumen Catheter, Piolax, Japan) was inserted to dilate the needle track and to exchange the previous guidewire into the 0.035 inch stiff one. The introducer of the covered Wallflex (10 mm-8cm) or covered Niti-S (10 mm-10cm) was inserted over the wire. Subsequently, the deep up-angle of the scope was taken to attach the gastric wall on the liver. After accommodating the introducer position, MS deployment was commenced. Before the complete release of the MS, the outer sheath was retracted deeply enough into the scope conduit, that was confirmed under the fluoroscopy. After the up-angle position and the elevator of the scope were relaxed, the introducer was extruded from the conduit. The spindle shape of the MS was observed under the endoscopic view because the counteraction conducted from the pushed introducer made the tip of the scope separate from the gastric wall.
**Results:** Between April 2011 and March 2016, we performed HGS using this procedure on 14 cases with malignant distal biliary stricture. In 13 cases (92.9%), the successful deployment was achieved. In a failure case, who had Child's reconstruction after the pancreatoduodenectomy, we could not attach the gastric wall to the liver enough. As only 8 cm MS was available at that time, we deployed 10 cm plastic stent transiently. MS migration into the stomach as a late complication was observed in two patients who had moderate cholangitis. However, these patients had no peritonitis and recovered after the deployment of another MS through the fistula.
**Conclusion:** The intra-conduit MS release method before the complete deployment is safe and feasible. MS of 10 cm length is preferable in this method.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## VC04 GASTRIC PERFORATION DUE TO DUODENAL-JEJUNAL BYPASS SLEEVE: NON-SURGICAL, ENDOSCOPIC REMOVAL PROCEDURE

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**Introduction:** The bariatric Duodenal-Jejunal Bypass Sleeve (DJBS) - Endobarrier TM - GI Dynamics, Inc., Lexington MA - is a temporary, endoscopically delivered device that consists of a proximal metallic self-expandable anchor, which is placed in the duodenal bulb, attached to a 60 cm sleeve that acts as a physical barrier to the mucosa up to the proximal jejunum. It constitutes a promising therapy strategy for weight loss as well as metabolic disorders associated with obesity [1–5]. It is, however, associated with a relatively high rate of adverse events, as well as rare but serious complications such as hematemesis, cholecystitis and duodenal perforation [5–7], some of which requiring surgical intervention.
**Aims & Methods:** We present the case of a 58-year-old male, who successfully underwent placement of a DJBS. Patient developed abdominal pain and postprandial fullness after 8 weeks. Endoscopic examination revealed metallic barbs migrated into the lesser curvature of the distal antrum, and a considerable amount of hyperplastic tissue in the duodenal bulb firmly adhered to the proximal metallic end of the DJBS. A two sessions endoscopic approach was then attempted for device removal. First, the pylorus and the proximal end of the device were dilated using a 20 mm hydrostatic balloon, and an over-the-scope fully covered 6 cm metallic stent was placed. Two weeks later, the stent was removed, and the excessive hyperplastic tissue was resected using a polypectomy snare. The proximal end of the plastic liner was then mobilized distally, as to disengage the metallic barbs from the gastric wall, exposing the removal drawstrings in the duodenal lumen.
**Results:** Device removal was then feasible according to the usual removal procedure: traction of one of the drawstrings using a custom grasper, followed by collapse of the metallic barbs into the removal cap, and complete extraction of the whole device. Immediate endoscopic evaluation showed no signs of major complications such as perforation of hemorrhage.
**Conclusion:** This case illustrates a serious complication of the DJBS and an endoscopic treatment technique that successfully prevented an invasive surgical intervention, demonstrating that DJBS removal may be possible even in very difficult scenarios.
**Disclosure of Interest:** M. Passos Galvão Neto: Consulting physician for GI DYNAMICS, Inc., Lexington MA.
All other authors have declared no conflicts of interest.

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## VC05 TUNNEL AND BRIDGE TECHNIQUE: A NOVEL APPROACH TO ENDOSCOPIC SUBMUCOSAL DISSECTION OF GIANT RECTAL POLYPS

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**Introduction:** Endoscopic submucosal dissection (ESD) is a safe and effective method for resecting large rectal polyps of over 2 cm. This technique facilitates en bloc dissection and leads to lower recurrence rates. However, ESD of giant laterally spreading tumours can be technically challenging.
**Aims & Methods:** We aim to demonstrate the use of a novel ESD 'tunnel and bridge' technique in the management of giant rectal polyps. A mucosal incision and a small degree of submucosal dissection is performed on the anal side followed by the caecal side of the lesion. This creates a 'polyp bridge'. Once the bridge has been fashioned, the submucosal dissection is extended from the anal side through to the caecal side of the polyp. Patient position change is utilised during the procedure, enabling gravity to hold the bridge up in place. The bridge ends are dissected using a scissor type knife to complete the polyp resection.
**Results:** This technique was demonstrated in a 63-year-old female with a 50 mm lateral spreading tumour – granular type in the rectum. There were no previous resection attempts. The lesion contained Kudo pit pattern IIIS and IIIL. Successful en bloc resection was achieved using the 'tunnel and bridge' technique with no complications. The histology from this lesion confirmed a tubular adenoma with low grade dysplasia. The adenoma was completely excised with no residual lesion present on follow up.
**Conclusion:** The 'tunnel and bridge' technique during endoscopic submucosal dissection of giant rectal polyps is a safe and viable method that enables time efficient resection. Further studies comparing this novel dissection technique to conventional ESD are needed to better understand and refine its role.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## VC06 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF A 25MM NEUROENDOCRINE TUMOUR OF THE GASTRIC BODY

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**Introduction:** Neuroendocrine Tumours (NETs) are neoplasms with predominant neuroendocrine differentiation that extend into the submucosa and sometimes involve the muscularis. Gastric NETs represent approximately 7% of all Gastroenteropancreatic NETs. Endoscopic resection has been shown as an effective method of treatment for Type I and II lesions as opposed to surgical resection. Traditionally endoscopic mucosal resection (EMR) was the preferred modality however this is now being replaced by endoscopic submucosal dissection (ESD) with improved outcomes.
**Aims & Methods:** To discuss the classification and management of Gastric Neuroendocrine tumours and to demonstrate endoscopic resection of a Gastric NET by ESD focusing on management of procedural complication especially major bleeding. This is a video of an ESD of 25 mm, Paris 0-Is, gastric NET (Type I) of the gastric body (greater curve).
**Results:** Complete endoscopic resection with histopathology confirming a well-differentiated Grade 2 Gastric NET.
**Conclusion:** ESD is an effective and safe technique for treatment of Gastric NETs (Type I and II). Major bleeding however can still occur despite prophylactic measures and endoscopistis must be aware of this risk.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## VC07 PROXIMALLY MIGRATED PANCREATIC STENT RETRIEVAL USING THE NEW SPYGLASS™ DS VISUALIZATION SYSTEM

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**Introduction:** Proximal migration of pancreatic stent (PS) is a complication described in patients with PS and its retrieval is a challenging situation considering that all known techniques are ''blind'' and developed for biliary stents(1).
**Aims & Methods:** A 36-year-old female was admitted in the hospital due to complete common bile duct dissection during a laparoscopic cholecystectomy. An ERCP was performed with biliary stent placement. During the procedure the main pancreatic duct was catheterized, so a straight, double-flared per side PS 5fr-7 cm was placed. The patient recovered uneventfully and biliary stent extraction and/or replacement were scheduled 3 months later. During the second ERCP, the biliary stent was identified and replaced but no PS was detected. Abdominal x-ray revealed the complete migration of the PS proximally inside the pancreatic duct. Pancreatic sphincterotomy was performed, followed by guide-wire cannulation of the main pancreatic duct. A biliary dilation balloon was repeatedly introduced over the wire, but failed to extract the stent. A single pigtail PS was then placed alongside the old PS and left for 5 days. An attempt followed to extract both stents at the same time, drifting the old stent while extracting the new one without success. Further attempts to retrieve the PS with biopsy forceps, a biliary stone extraction balloon and again, with biliary dilation balloon, failed as well. Subsequently, direct pancreatoscopy with the Spyglass™ visualization system (Boston Scientific) was performed. The distal end of the stent was visualized, but multiple attempts to grab the stent with the SpyBite™ forceps (Boston Scientific) failed due to the position of the PS and poor SpyBite deployment. In the final procedure, the new Spyglass™ DS (Boston Scientific) was used. The image quality was far superior compared to its predecessor. The distal end of the PS was clearly identified and Spybite was easier to introduce and deploy. Several attempts were done in order to change the stent's tip position. Then the tip was grabbed and successfully removed. No procedure-related complications occurred except for asymptomatic amylasemia and the patient was discharged two days later.
**Results:** Proximally migrated pancreatic stents can be effectively identified grasped and retrieved with the new Spyglass™ DS system.
**Conclusion:** The high image quality, the adequate manoeuvrability and ease of use that the new system offers under direct visualization, enables an alternative safe salvage technique when conventional methods of stent retrieval have failed.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

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## VC08 ENDOSCOPIC MUCOSAL RESECTION OF GIANT FLAT POLYP EXCLUSIVELY CLOSED WITH A SURGICAL HAEMOSTATIC AGENT

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**Introduction:** An asymptomatic 72-year-old man was diagnosed with colonic polyps in the colorectal-cancer-screening program. The biggest polyp was localized in the proximal transverse colon with a diameter of 5 cm and characterized as lateral spread with IIIL/ IV based in Kudós classification, II/ IIa Sano and LST-G IIa+Is under Pariśs classification. The polyp was resected in ''piece meal'' (3 pieces) and fulgurated with Argon plasma coagulation (APC) over the suspicious remains areas and also over the proximal edge. Immediately after finished the resection the scarf was covered with a surgical haemostatic agent (PURASTAT®), No adverse event was presented nor after immediately post-procedure and neither in the follow-up.
**Aims & Methods:** Closing the scarf after mucosectomies reduces significantly secondary events such as immediately bleeding or delay bleeding. However in giant polyps it would be impossible to close with the traditional systems as through-the- scope clips or over-the-scope clips and could develop late stricture. For this reason, we used the PuraStat®, which is a transparent, slightly viscous synthetic peptide solution that is marked as a surgical haemostat agent. Upon contact with blood, the peptide solution instantaneously self-assembles a hydrogel barrier, sealing open blood vessels naturally to accomplish complete haemostasis.
**Results:** The histology of resection pieces were tubule-villous adenoma with high-grade dysplasia (Haggitt 0), with free edge.
**Conclusion:** Thus this case is a unique example exemplifying the safety and efficiency to use of this new method to prevent the bleeding after large mucosectomy and reduces the rate of delay strictures. In addition this report showed a new, easy and fast technique to applied the haemostatic agent.
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## VC09 THE INSERTION OF A PERCUATENOUS ENDOSCOPIC SIGMOIDOSTOMY TUBE

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**Introduction:** We present a video demostration of insertion of a percutaneous endoscopic sigmoidostomy tube and a brief overview of possible problems and after care.
**Aims & Methods:** The main indications are recurrent sigmoid volvulus and chronic pseudo-obstruction. It may also be used for chronic constipation to administer enemas.
**Results:** It is a safe procedure with minimal morbidity for commonly encountered problems often necessitating repeat hospitalisation.
**Conclusion:** Percutaneous endoscopic sigmoidostomy offers an alternative treatment for patients who have tried conventional treatment options without success. Traditional treatment options for sigmoid volvulus and pseudo-obstruction comprise endoscopic decompression and/or open resection. However, these management options have varying success with endoscopic decompression having a recurrence rate of approximately 40% and open resection may be contraindicated for frail, elderly patients or the severly immunocompromised. Please see video:
https://youtu.be/wD1bo1-toLE
**Disclosure of Interest:** All authors have declared no conflicts of interest.

## VC10 HIGH MAGNIFICATION DIAGNOSIS AND TREATMENT OF ESOPHAGEAL INTRAEPITHELIAL SQUAMOUS CELL CARCINOMA

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**Introduction:** Endoscopic submucosal dissection (ESD) is the standard treatment for intraepithelial esophageal squamous tumors[1]. A high-quality preliminary endoscopy of eligible lesion is essential for a satisfactory outcome. For this purpose, the classification of intrapapillary capillary loop arrangement and the iodine staining characteristics (IPCL)[2] is a reliable predicting tool. We report our experience using a new generation gastroscope for the preliminary assessment and subsequent endoscopic resection of intraepithelial esophageal squamous cell carcinoma.

**Aims & Methods:** A 59-year-old man with a relevant history of alcohol abuse, underwent upper endoscopy. A gastroscope, equipped with 3rd generation Narrow Band Imaging (NBI) and high magnification zooming lever (Olympus H290Z, Japan) was employed. A cylindrical soft hood was employed for both the assessment and resection of the lesion, which was recognized under white light. The iodine staining and IPCL characteristics were employed to determinate the borders and the staging of the lesion. A glycerol solution was employed to lift the lesion border. The dissection was performed using a water-jet assisted dual knife (Olympus, Japan) connected to a manual infusion system (Figure 1a-b). Coagulation forceps and short clips were employed for preventive coagulation of visible vessels

**Results:** The normal iodine staining was lost in the majority of the lesion and partially in the surrounding inflamed mucosa (figure 2b). Therefore, the neoplastic borders were marked according to the IPCL findings (Figure 2a-d). We experienced a satisfactory feasibility by using the same endoscope for ESD, avoiding scope change and easily visualizing vascular structure even in difficult positions by using the zoom lever (figure 2e-g). The ESD procedure duration was 160 minutes. No intra-procedural or short-term adverse events were reported. The length of the stay was 5 days. The histopathology confirmed the R0 endoscopic resection of a mild differentiated intraepithelial esophageal squamous carcinoma (T1a)

**Conclusion:** The new generation zoom endoscope allowed an optimal observation of early squamous cell esophageal neoplasm characteristics and a feasible endoscopic resection in this preliminary experience. The adjustable zoom resulted in a continuous high quality view, which facilitated some procedural steps of the endoscopic resection. For the resection of distal esophageal lesions, a standard "J" endoscope with a major retroflection bending capacity may be preferred.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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